



Dkt. No. 96700/860

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : David S. Lawrence
Serial No. : 10/755,086
Filed : January 9, 2004
For : FLUORESCENT ASSAYS FOR PROTEIN KINASES
Art Unit : 1657
Examiner : Clark D. Petersen
Customer No. : 1912

DECLARATION OF DAVID S. LAWRENCE UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, David S. Lawrence, hereby declare as follows:

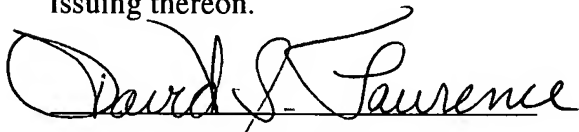
1. I am the inventor of the subject matter claimed in U.S. Patent Application No. 10/755,086. I am currently a Professor in the Department of Biochemistry at Albert Einstein College of Medicine of Yeshiva University, Bronx, New York.
2. I understand that some claims pending in the application are rejected under 35 U.S.C. §102(a) as being anticipated by the January 14, 2002 Journal of Biological Chemistry (JBC) Papers in Press publication entitled "Real Time Visualization of Protein Kinase Activity in Living Cells," which is authored by Ren-Hwa Yeh, Xiongwei Yan, Michael Cammer, Anne R. Bresnick and myself ("the JBC Article").
3. Ren-Hwa Yeh, who at that time was a postdoctoral fellow in my laboratory, was included as an author on the JBC Article because he assisted in performing the cell-based studies of the sensors as per my direction. Xiongwei Yan, who at that time was a postdoctoral fellow in my laboratory, was included as an author on the JBC Article because he assisted in synthesizing and screening the library of potential protein kinase sensors as per my direction. Michael

Cammer, who at that time was Director of Light Microscopy and Image Analysis in the Analytical Imaging Facility at the Albert Einstein College of Medicine, was included as an author on the JBC Article because he assisted in training Ren-Hwa Yeh in microinjection techniques and helped analyze data as per my direction. Anne R. Bresnick, who is a faculty member in our department, was included as an author on the JBC Article because she provided advise on cell-based studies. None of Ren-Hwa Yeh, Xiongwei Yan, Michael Cammer or Anne R. Bresnick contributed to the conception of the invention claimed in the present application.

4. I also understand that some pending claims are rejected under 35 U.S.C. §103(a) as being unpatentable over the March 22, 2002 Journal of the American Chemical Society (JACS) Web publication entitled "Design and Synthesis of a Fluorescent Reporter of Protein Kinase Activity," which is authored by Chien-An Chen, Ren-Hwa Yeh and myself ("the JACS Article"), in view of Haugland et al. (U.S. Patent No. 5,635,608).

5. Chien-An Chen, who at that time was a postdoctoral fellow in my laboratory, was included as an author on the JACS Article because he synthesized the sensors as per my direction. Ren-Hwa Yeh, who at that time was a postdoctoral fellow in my laboratory, was included as an author on the JACS Article because he assisted in performing the enzyme-based studies as per my direction. Neither Chien-An Chen nor Ren-Hwa Yeh contributed to the conception of the invention claimed in the present application.

6. I hereby declare that all statements made herein and of my knowledge are true and that all statements made on information and belief are believed to be true; and I further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


David S. Lawrence

Dated: 4/3/07



Dkt. No. 96700/860

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No. : 10/755,086
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DECLARATION OF DAVID S. LAWRENCE UNDER 37 C.F.R. §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

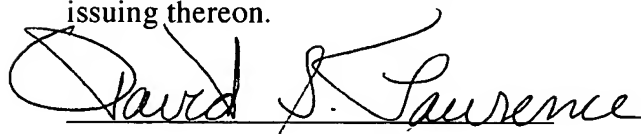
I, David S. Lawrence, hereby declare as follows:

1. I am the inventor of the subject matter claimed in U.S. Patent Application No. 10/755,086. I am currently a Professor in the Department of Biochemistry at Albert Einstein College of Medicine of Yeshiva University, Bronx, New York.
2. I understand that some claims (Claims 49-69, 71-77, 81, 83, 86-90, 95, 97-100, 102-109, 112, 114, 116-119, 122-123, 127-131, 133 and 134) pending in the application are rejected under 35 U.S.C. §102(e) as being anticipated by Nguyen et al., U.S. Patent Application Publication No. US2004/0166553, which has a priority date of November 18, 2002.
3. I refer the Examiner to two publications already of record in the Office Action issued on December 15, 2006 during the prosecution of this application to demonstrate that I had reduced aspects of the claimed invention to practice in the United States before the November 18, 2002 priority date of Nguyen et al., U.S. Patent Application Publication No. US2004/0166553. The experiments described in these publications were carried out in my laboratory in the Department of Biochemistry at Albert Einstein College of Medicine, Bronx, New York.

The first publication is the January 14, 2002 Journal of Biological Chemistry (JBC) Papers in Press publication entitled "Real Time Visualization of Protein Kinase Activity in Living Cells," which is authored by Ren-Hwa Yeh, Xiongwei Yan, Michael Cammer, Anne R. Bresnick and myself. The paper appeared in print form in the March 29, 2002 issue of The Journal of Biological Chemistry (Vol. 277, No. 13, pages 11527-11532) ("the JBC Article"). I attach hereto a copy of the Data Supplement for that publication, which was available online at the time of publication. The attached Data Supplement Table (124 pages) corresponds to Table 3 of the application. The JBC Article provides support for subject matter recited in at least the following claims that are rejected as anticipated by Nguyen et al., U.S. Patent Application Publication No. US2004/0166553: Claims 49-51, 61, 63-65, 67-69, 72-74, 81, 88, 90, 98-100, 103-105, 112, and 117-119.

The second publication is the March 22, 2002 Journal of the American Chemical Society (JACS) Web publication entitled "Design and Synthesis of a Fluorescent Reporter of Protein Kinase Activity," which is authored by Chien-An Chen, Ren-Hwa Yeh and myself. The paper appeared in print form in J. Am. Chem. Soc. 124: 3840-3841, 2002 ("the JACS Article"). I attach hereto a copy of the Supporting Information (10 pages) for that publication, which was available online at the time of publication. The JACS Article provides support for subject matter recited in at least the following claims that are rejected as anticipated by Nguyen et al., U.S. Patent Application Publication No. US2004/0166553: Claims 49, 61, 63-69, 72-74, 81, 83, 89 (see in particular attached Supporting Information), 90, 95, 97-100, 103-105, 112, 114, 116-119, 127-131, and 133-134.

4. I hereby declare that all statements made herein and of my knowledge are true and that all statements made on information and belief are believed to be true; and I further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


David S. Lawrence

Dated: 4/3/07



J. Biol. Chem., Vol. 277, Issue 13, 11527-11532, March 29, 2002

Data Supplement for Journal of Biological Chemistry: Volume 277, Issue 13 -- Page 11527

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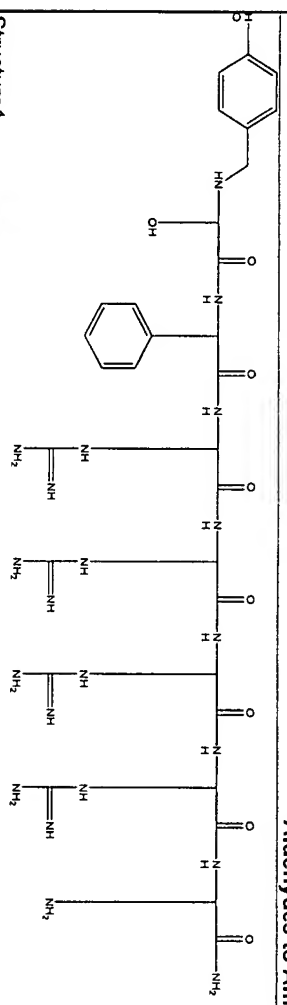
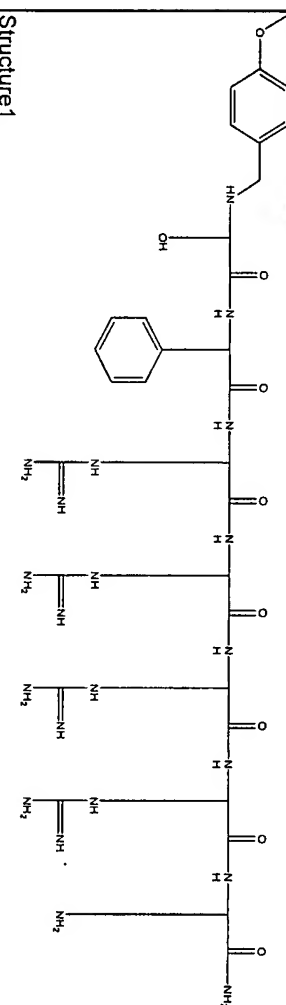
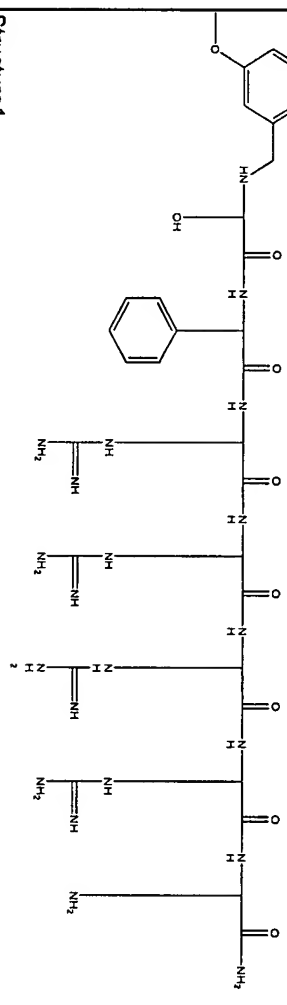
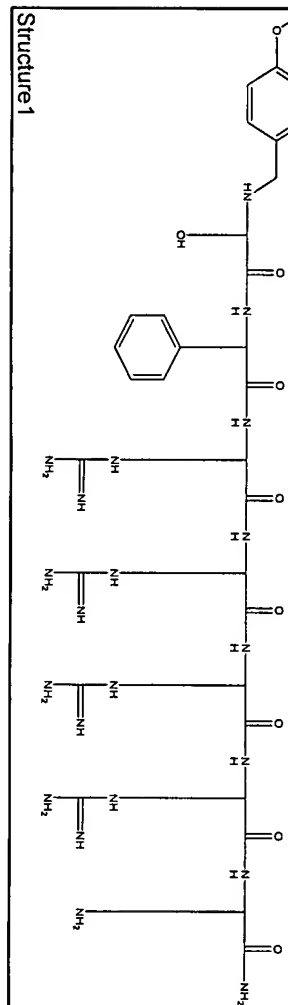
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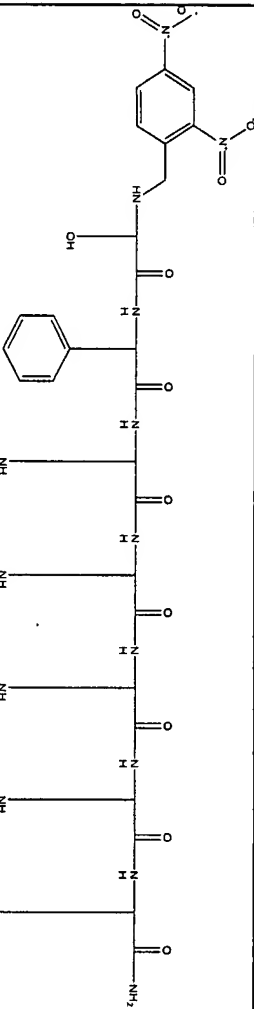
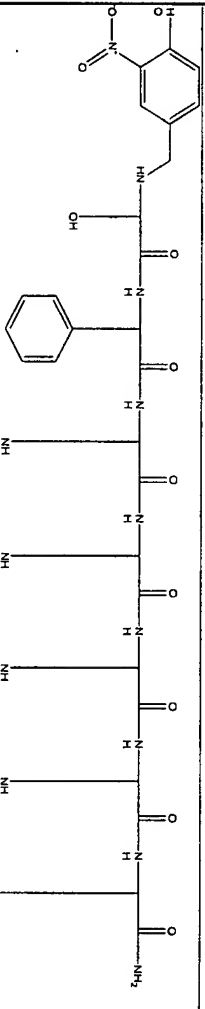
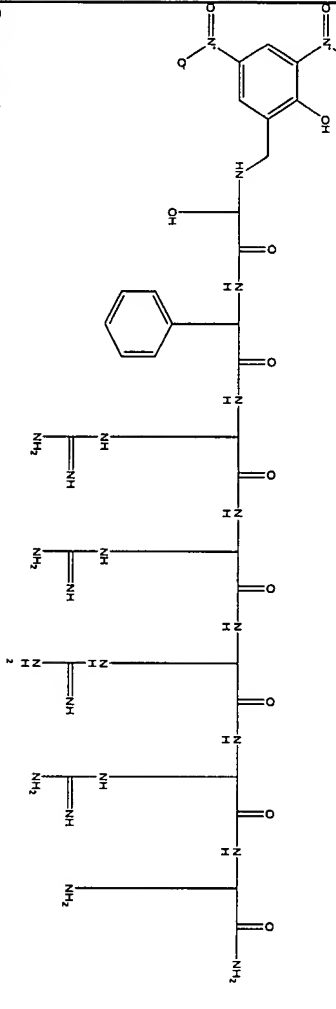
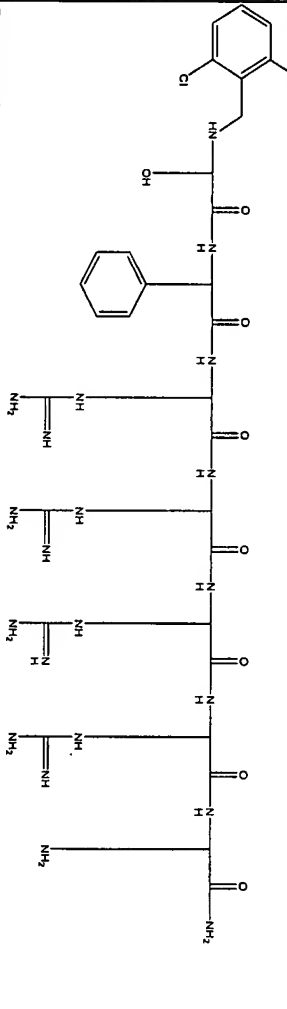
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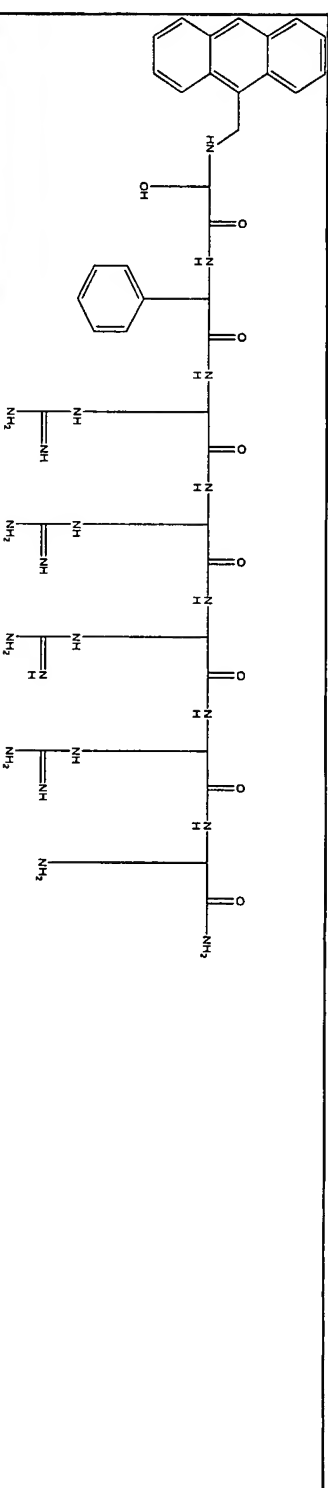
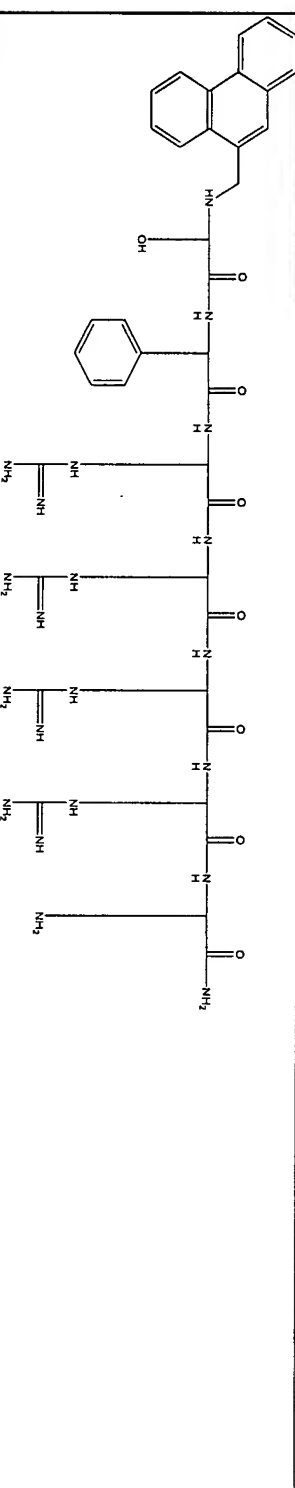
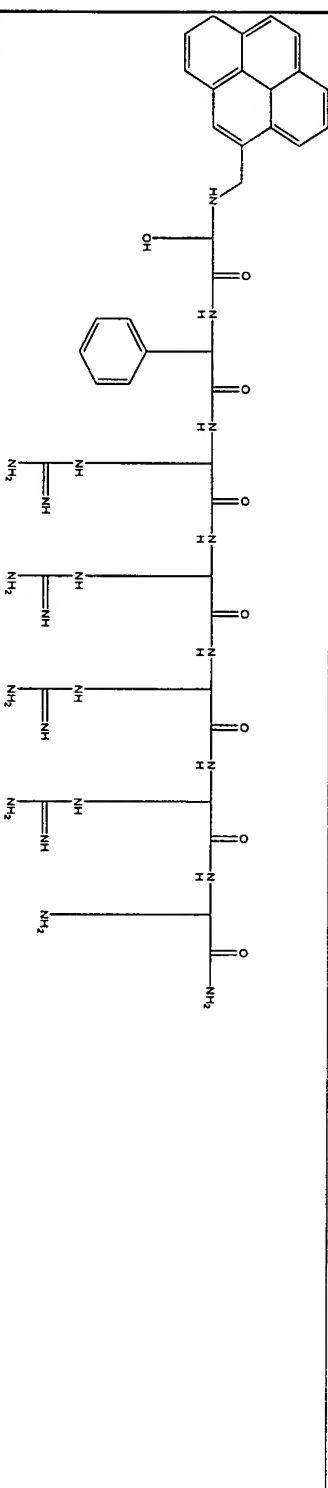
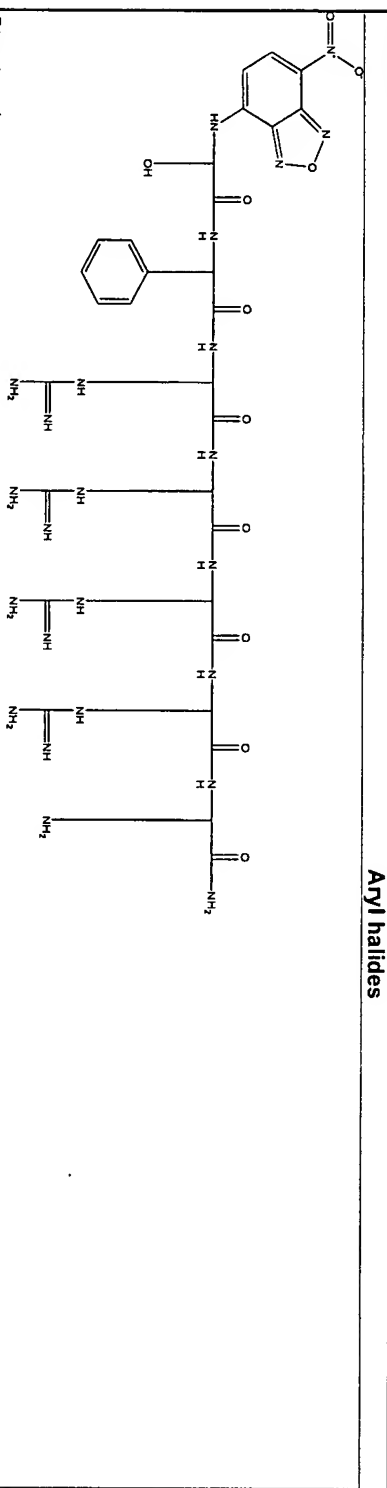
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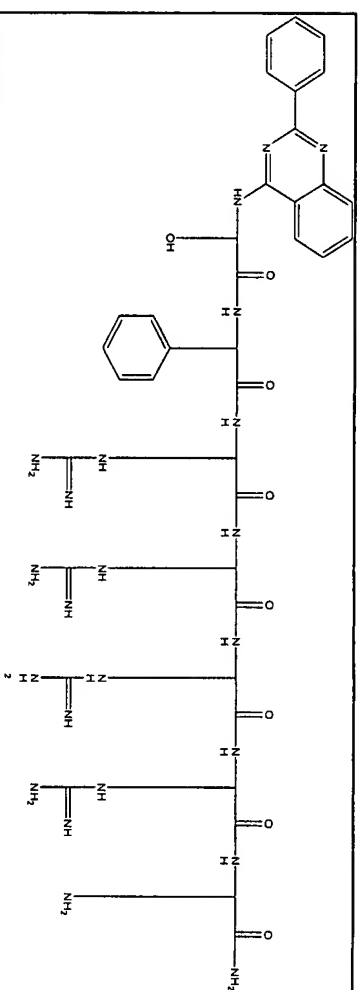
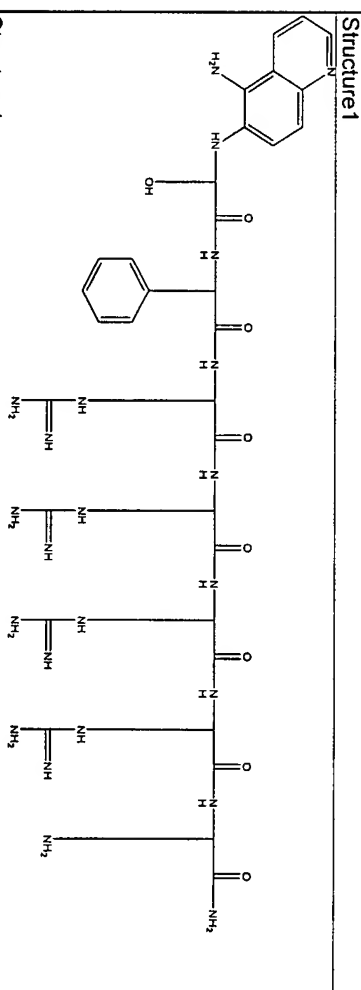
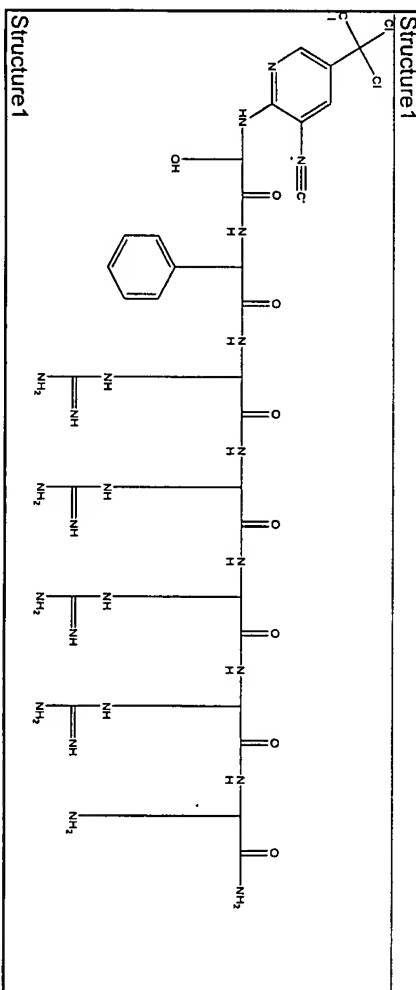
STRUCTURE			formula	molweight	%
Aldehydes to Amines					
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Structure1					
			C50H85N21O9	1124.3568	<10%
Structure1					
			C50H85N21O10	1140.3562	<10%
Structure1					
			C51H87N21O10	1154.383	<10%
Structure1					

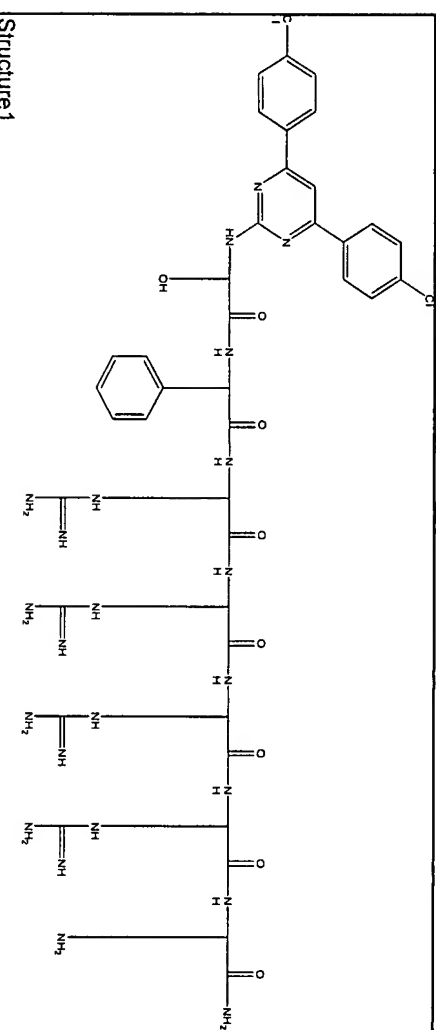
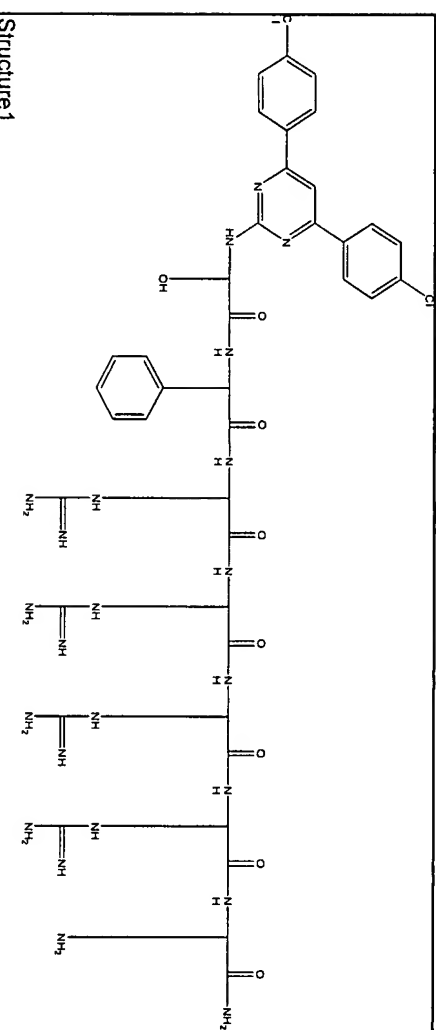
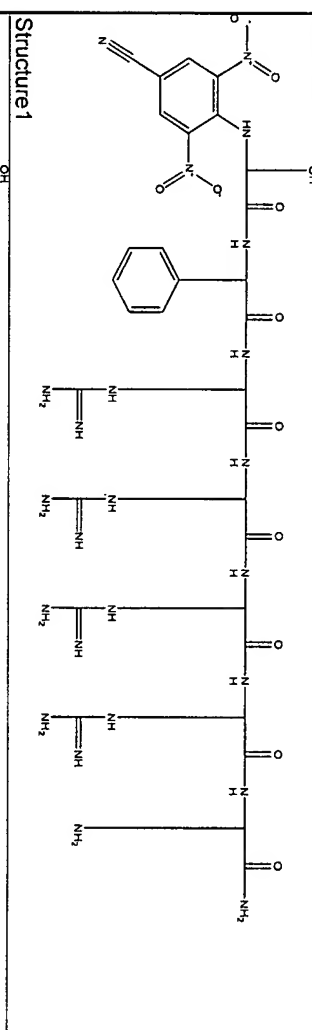
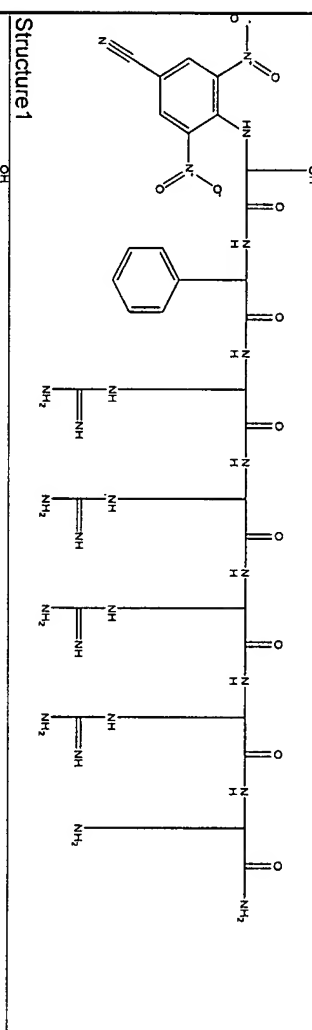
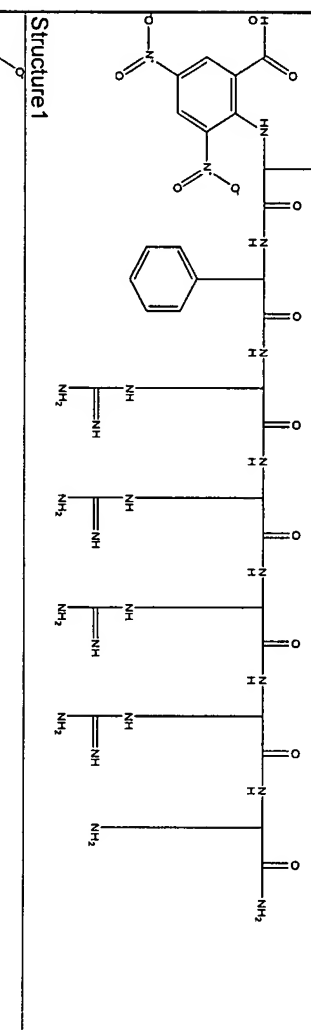
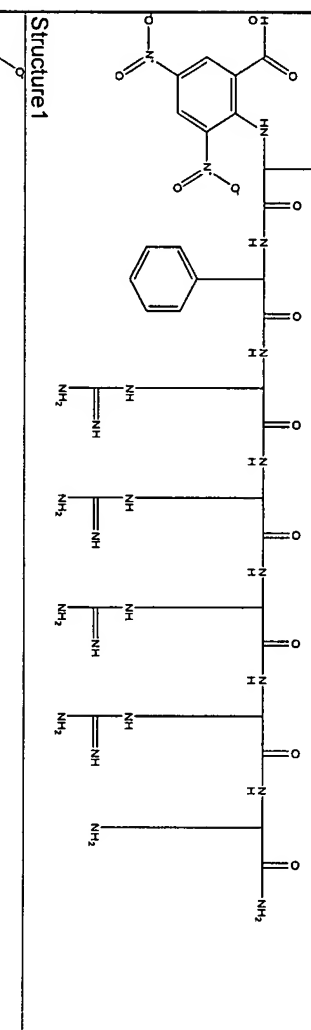
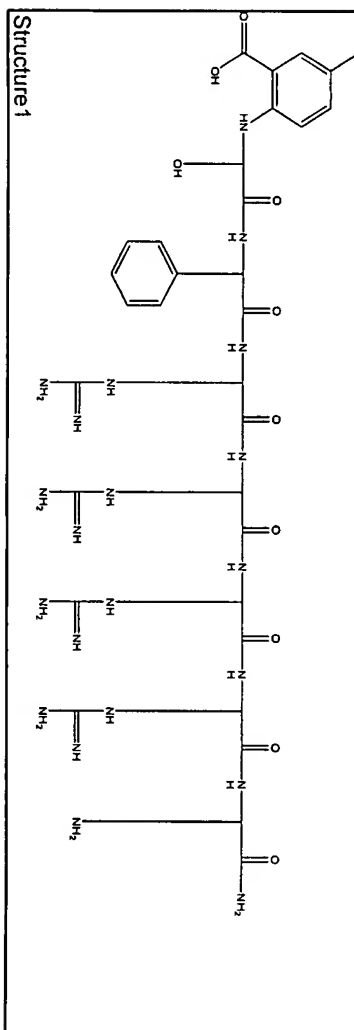
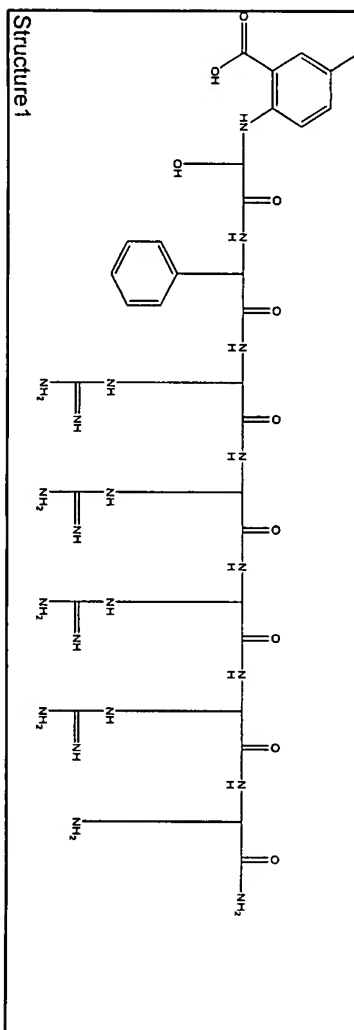
 <p>Structure 1</p>	C49H81Cl2N2O13	1184.3258	<10%
 <p>Structure 1</p>	C49H82N2O11	1155.3276	<10%
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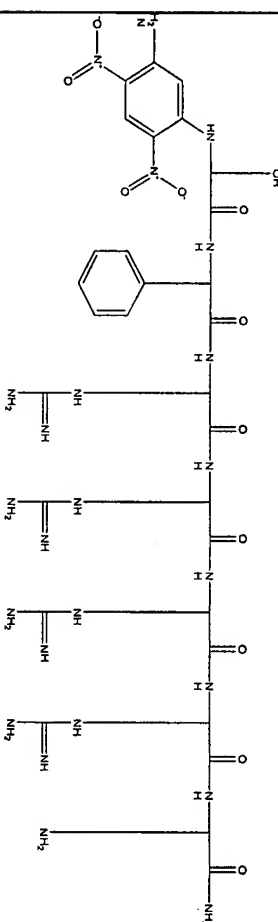
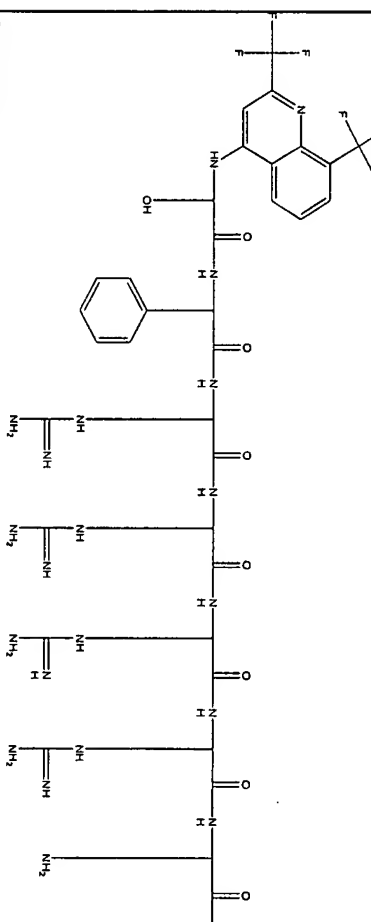
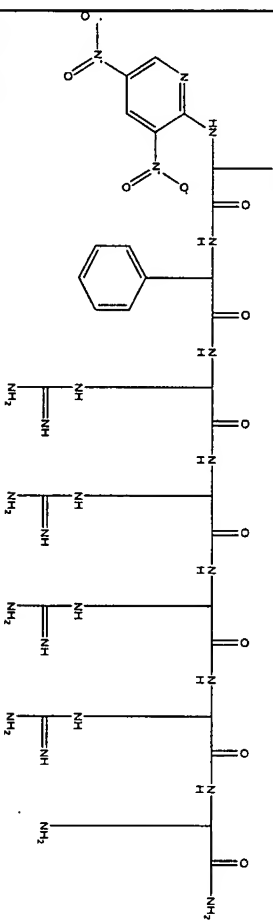
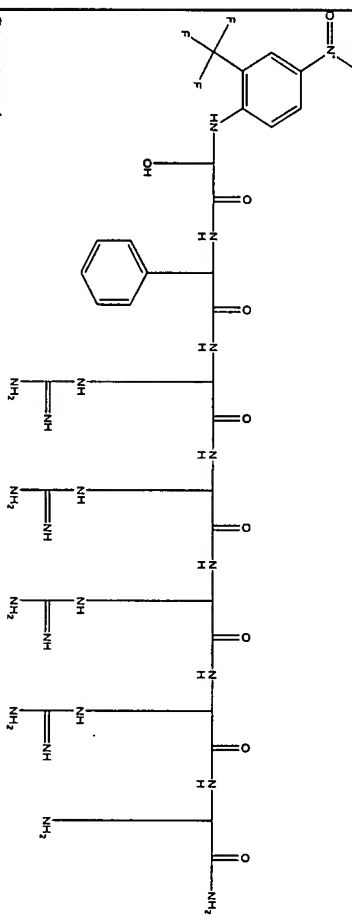
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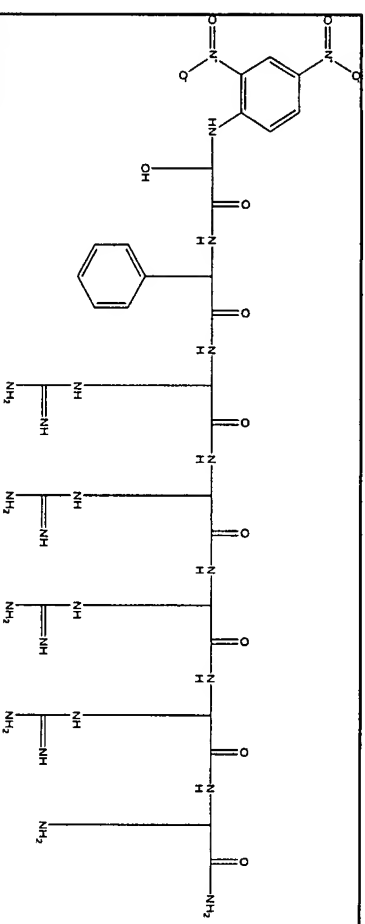
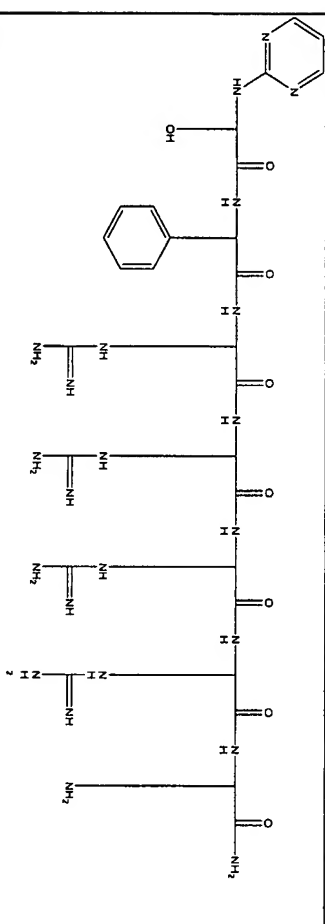
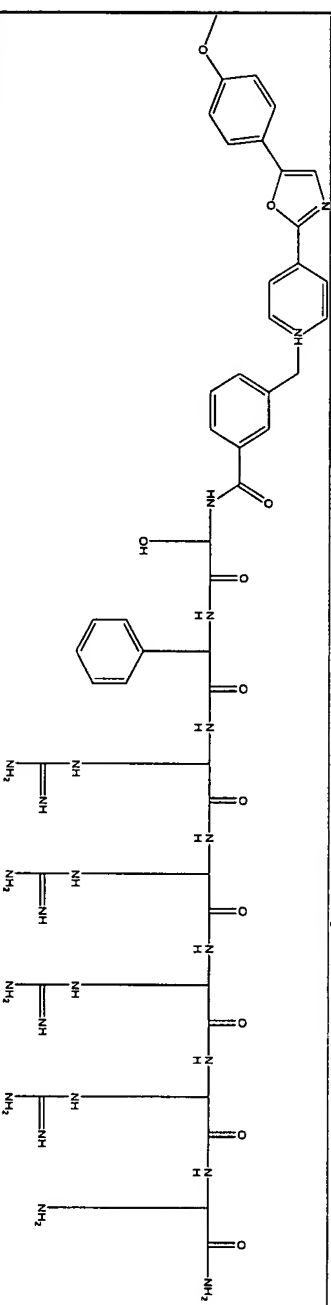
 <p>Structure 1</p>	C57H87N21O8	1194.4502 <10%
 <p>Structure 1</p>	C57H87N21O8	1194.4502 <10%
 <p>Structure 1</p>	C59H89N21O8	1220.488 <10%
 <p>Structure 1</p>	C48H78N24O11	1167.2984 150%

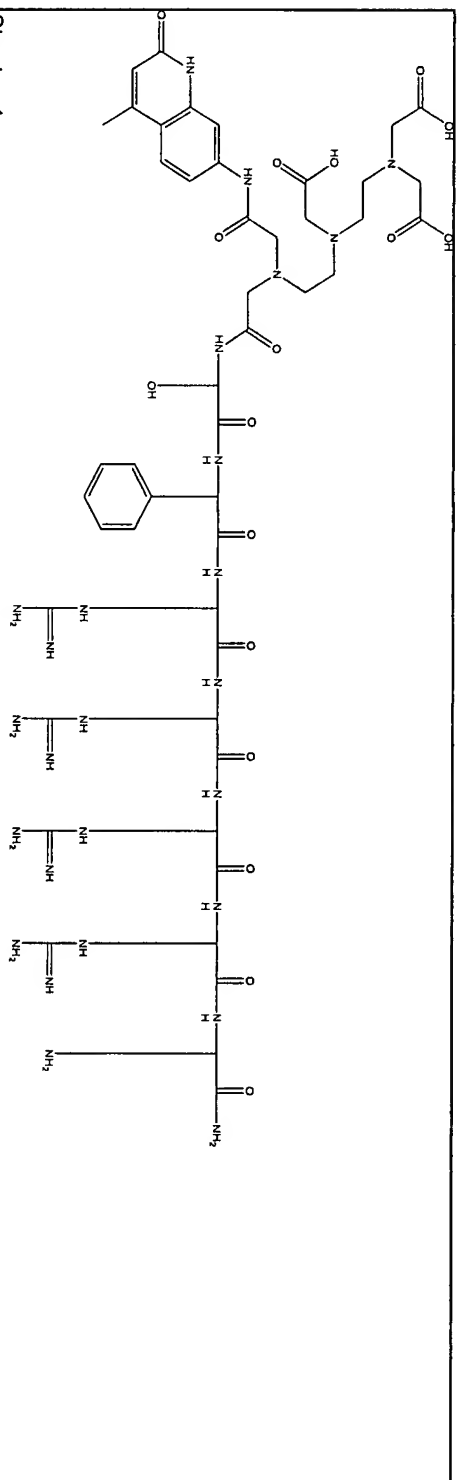
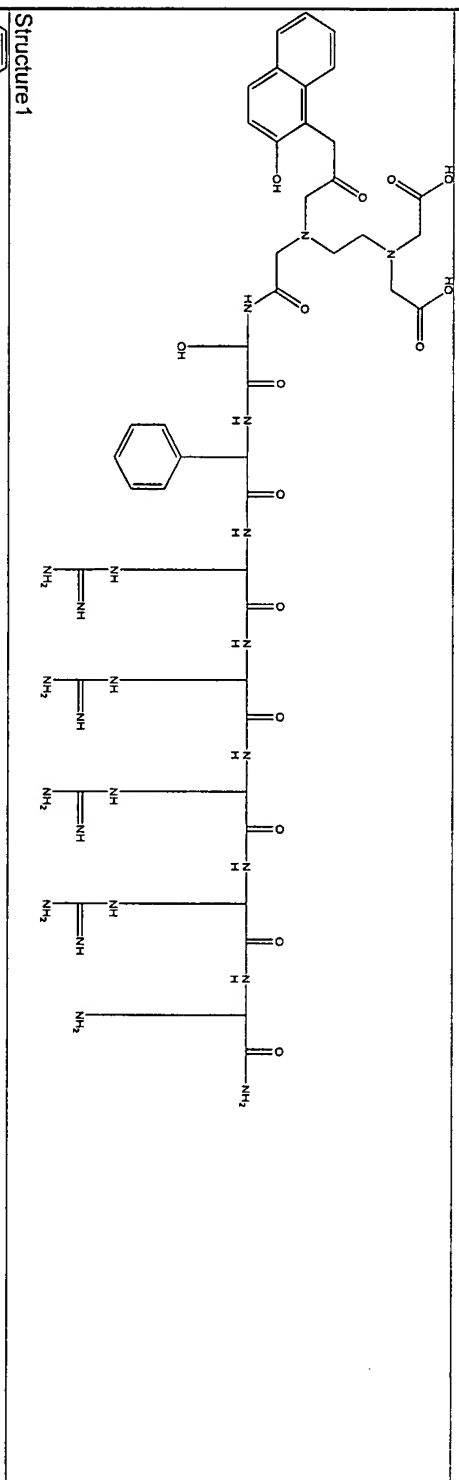
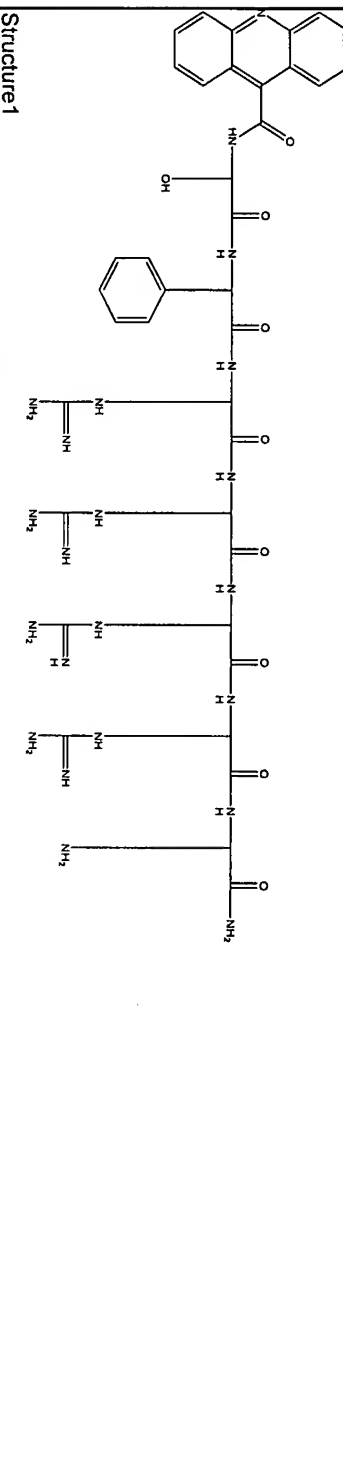
Aryl halides

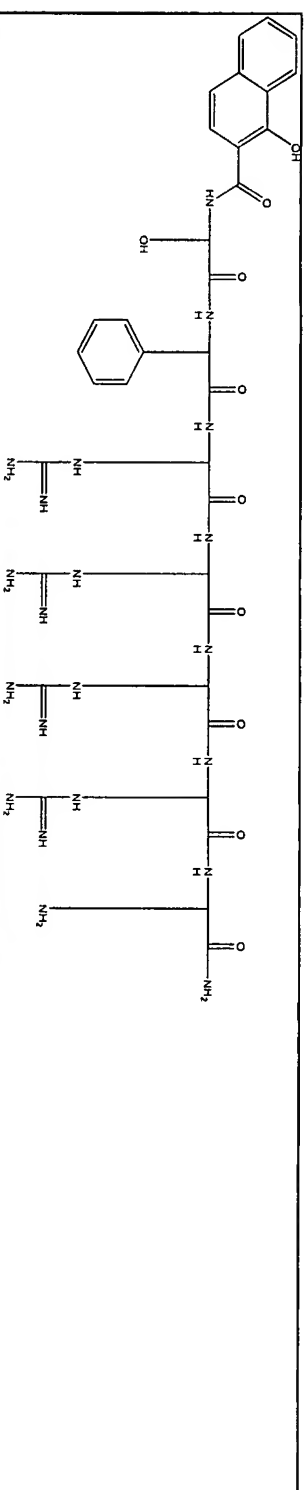
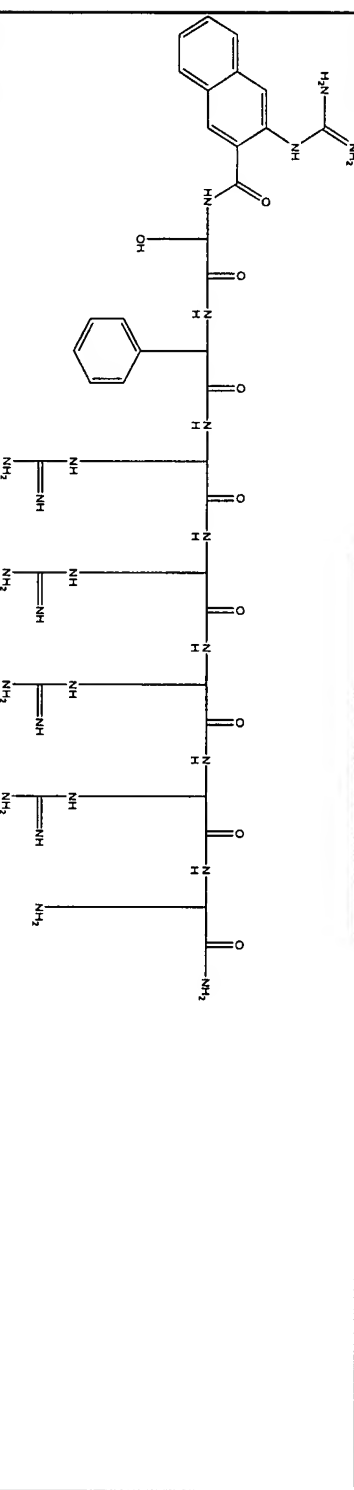
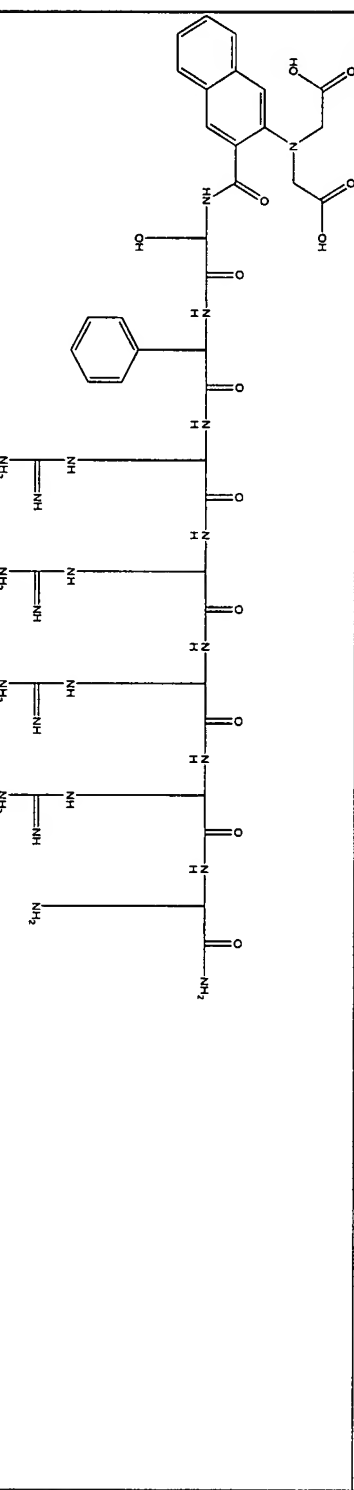
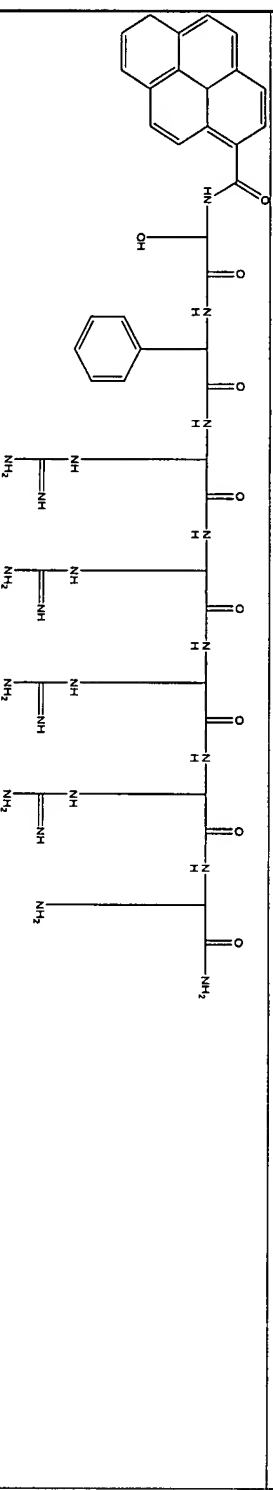
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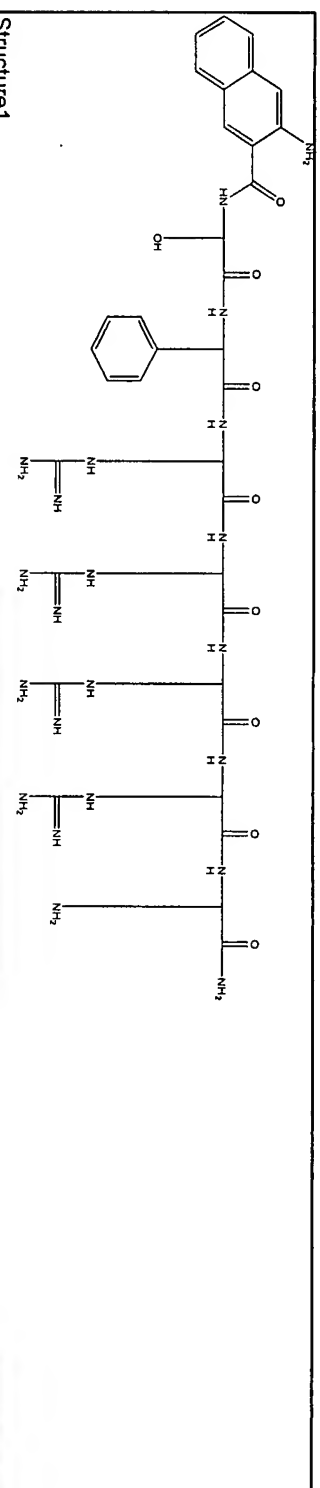
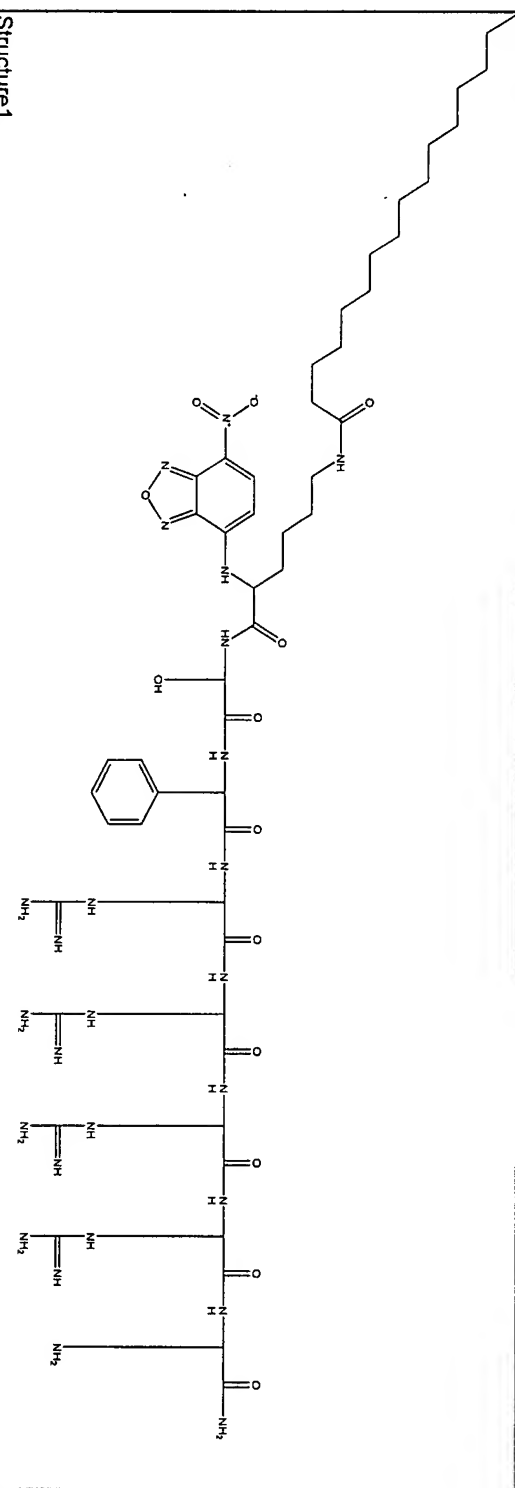
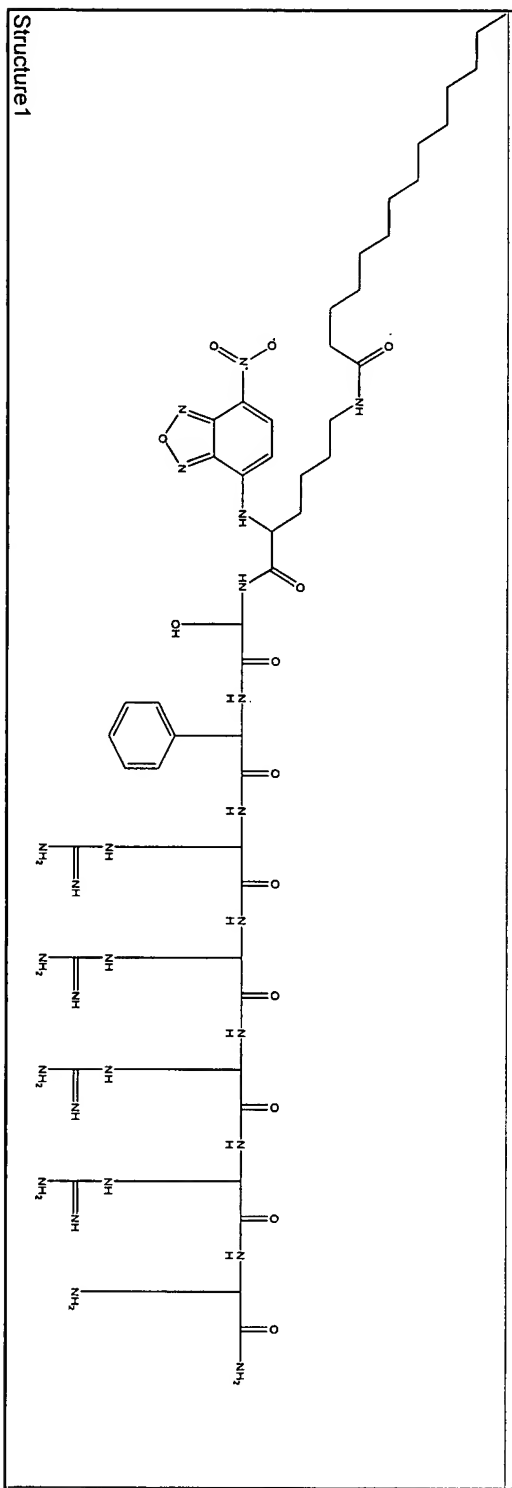
 <p>Chemical structure of C58H85Cl2N23O8, showing a complex molecule with multiple amide and urea groups, a phenyl ring, and two 4-chlorophenyl groups attached to a pyrimidine ring.</p>			
<p>Structure 1</p> 	C58H85Cl2N23O8	1303.3648	<10%
 <p>Chemical structure of C49H78N24O12, showing a complex molecule with multiple amide and urea groups, a phenyl ring, and a 4-cyano-2,6-dinitrophenyl group.</p>			
<p>Structure 1</p> 	C49H78N24O12	1195.3088	<10%
 <p>Chemical structure of C49H79N23O14, showing a complex molecule with multiple amide and urea groups, a phenyl ring, and a 2,6-dinitro-4-(hydroxymethyl)phenyl group.</p>			
<p>Structure 1</p> 	C49H79N23O14	1214.3088	<10%
 <p>Chemical structure of C49H80N22O12, showing a complex molecule with multiple amide and urea groups, a phenyl ring, and a 2-nitro-4-(hydroxymethyl)phenyl group.</p>			
<p>Structure 1</p> 	C49H80N22O12	1169.3112	<10%

<p>Structure 1</p> 	C48H80N24O12	1185.3136 <10%
<p>Structure 1</p> 	C53H80F6N22O8	1267.348 <10%
<p>Structure 1</p> 	C47H78N24O12	1171.2868 <10%
<p>Structure 1</p> 	C49H79F3N22O10	1193.2997 <10%

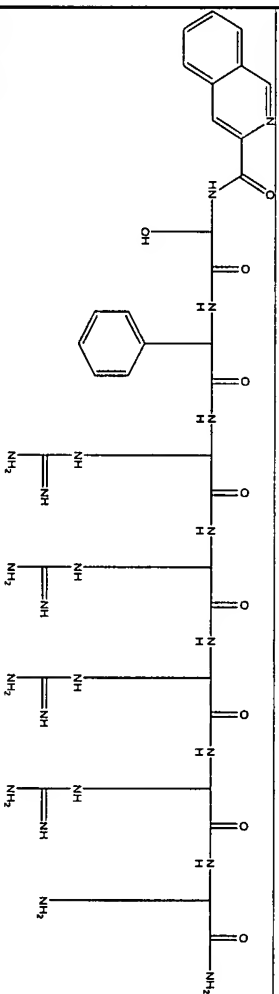
<p>Structure 1</p> 	C48H79N23O12	1170.299 <10%
<p>Structure 1</p> 	C46H79N23O8	1082.2794 <10%
Carboxylic Acids		
<p>Structure 1</p> 	C65H95N23O11	1374.613 <10%

<p>Structure 1</p> 	<p>C66H106N26O17</p>	<p>1535.7274</p>	<p><10%</p>
<p>Structure 1</p> 	<p>C63H99N23O15</p>	<p>1418.6202</p>	<p><10%</p>
<p>Structure 1</p> 	<p>C56H84N22O9</p>	<p>1209.4216</p>	<p>20%</p>

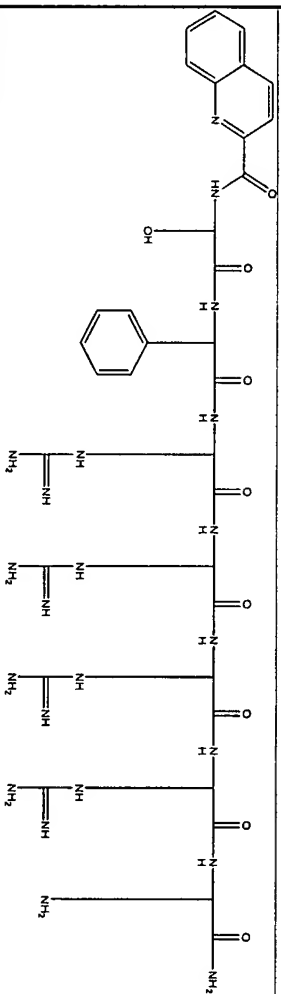
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	C54H87N24O9+	1216.4367 <10%
	C57H88N22O13	1289.4618 <10%
	C59H87N21O9	1234.4716 <10%

	C53H84N22O9	1173.3686	<10%
	C70H120N26O13	1533.8644	<10%
	C68H116N26O13	1505.8308	<10%

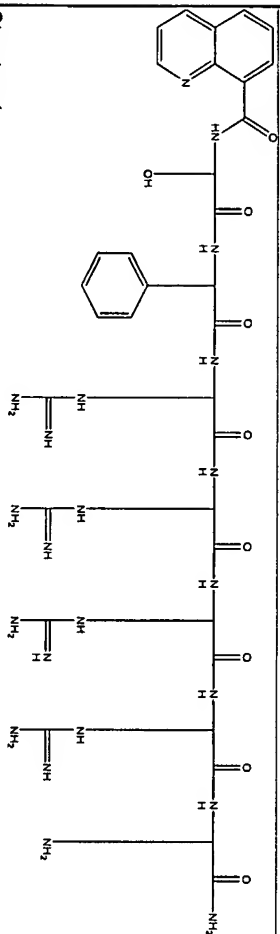
1462.63	<10%
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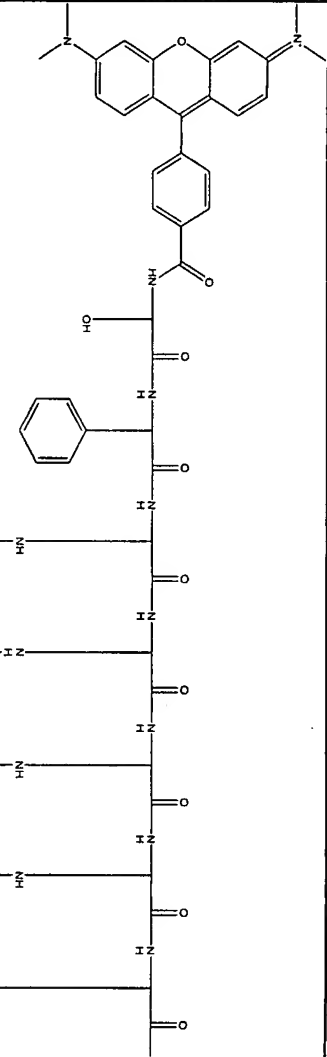
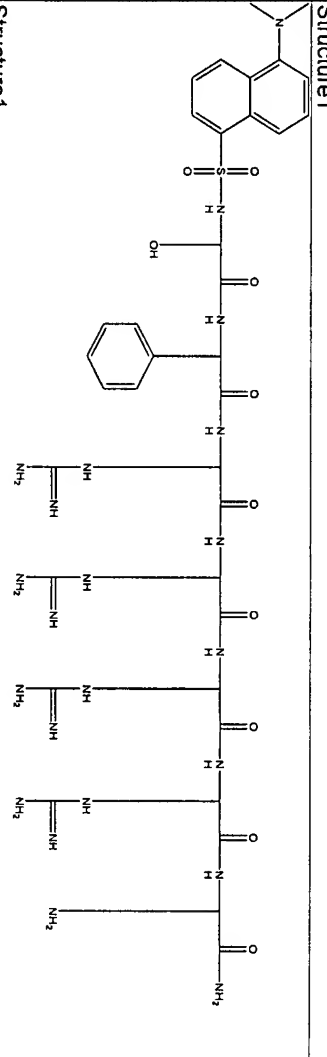
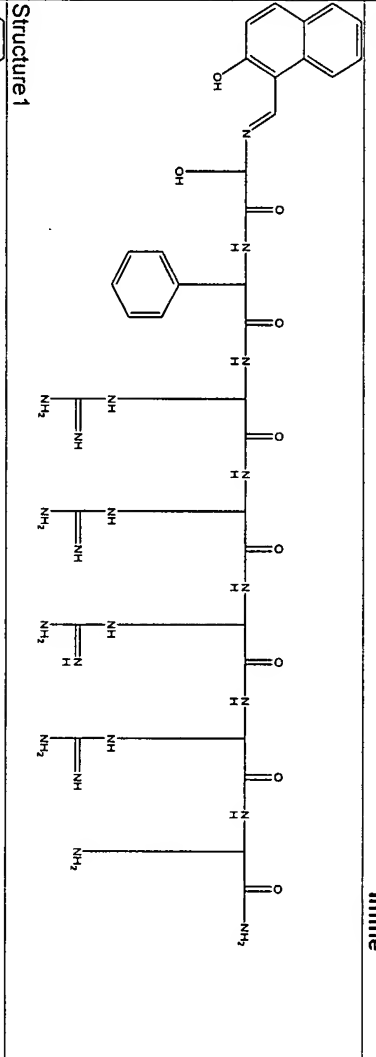
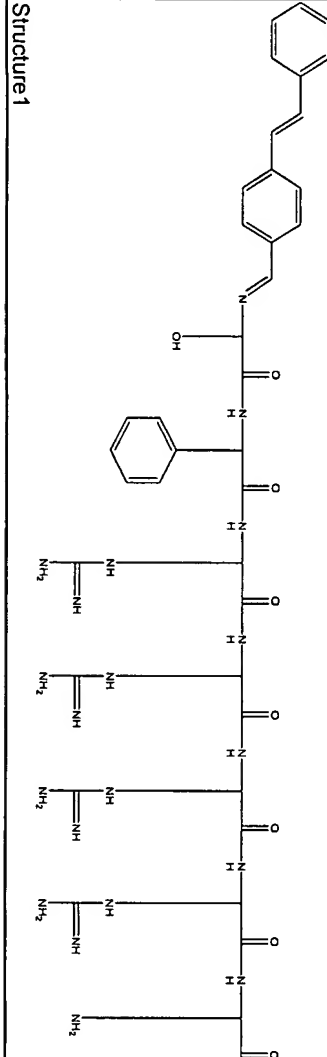
1159.3618	<10%
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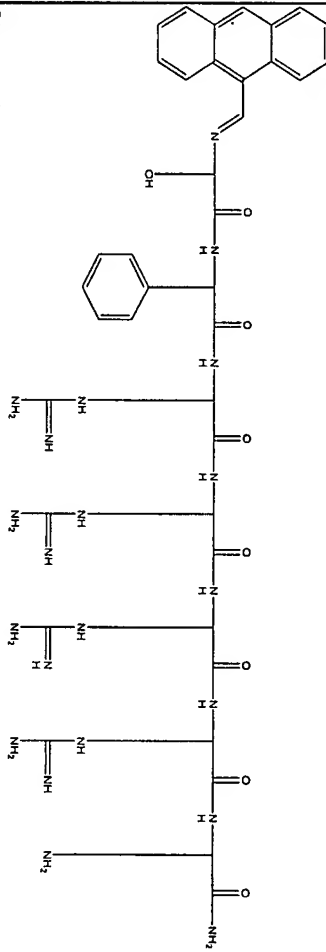
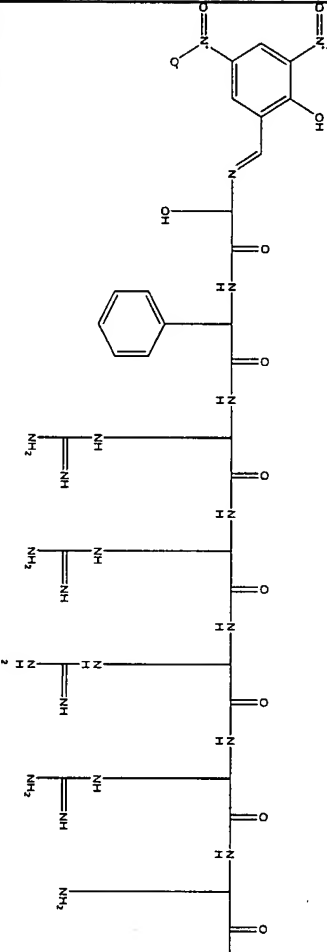
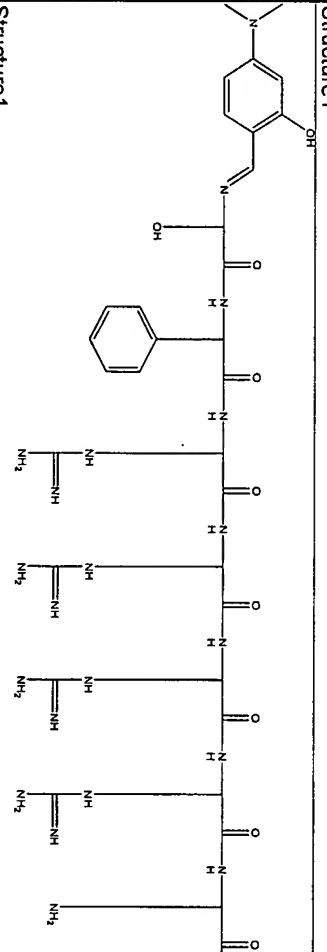
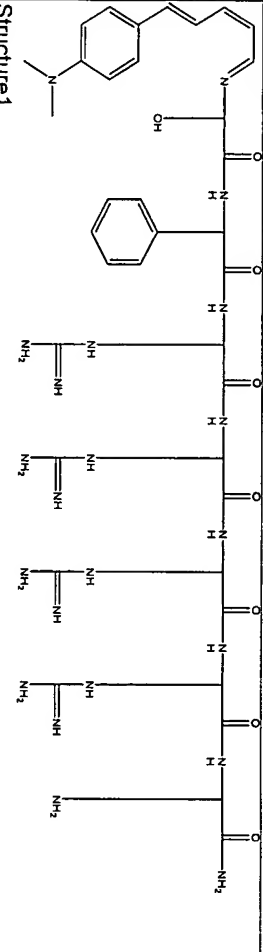


1159.3618 <10%

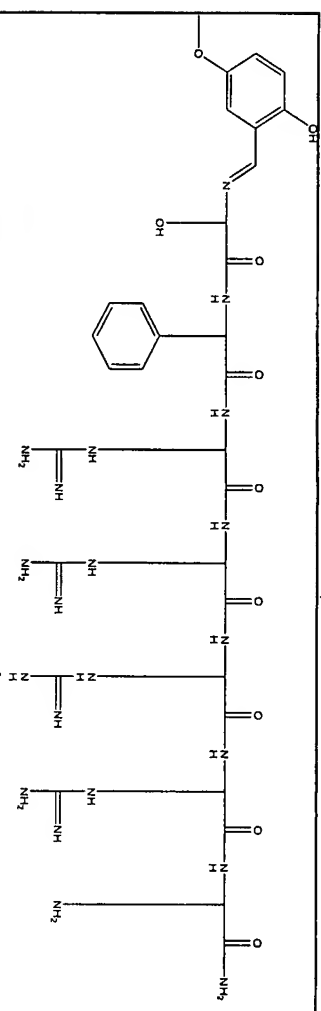
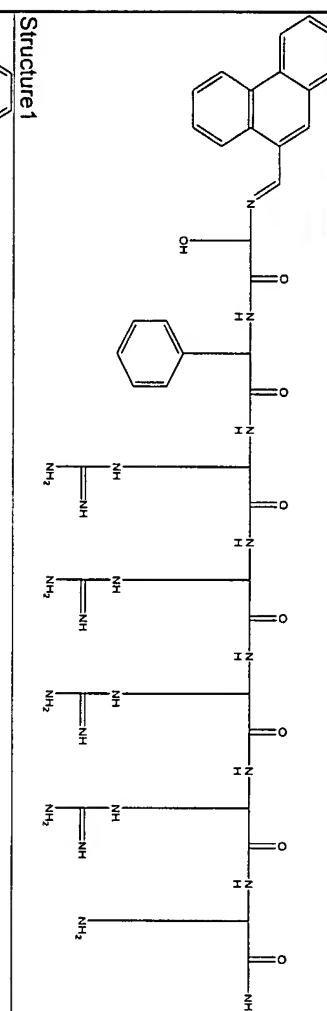
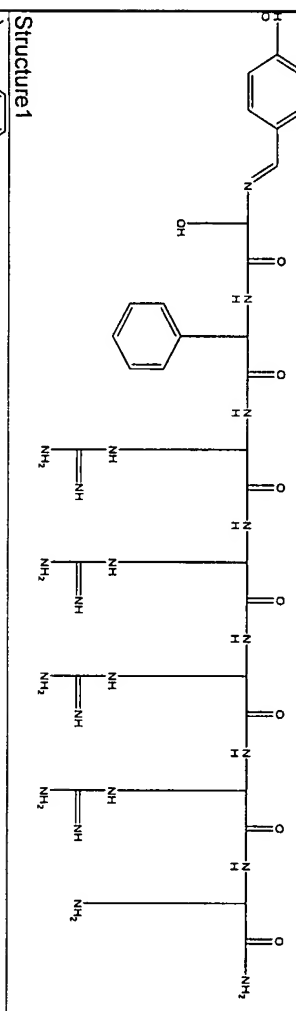
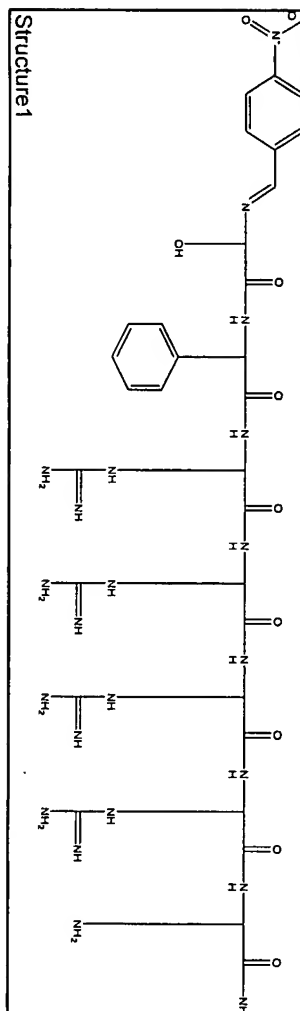


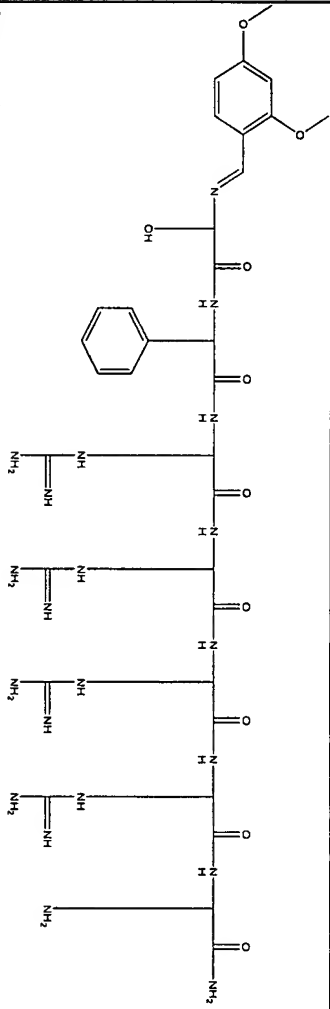
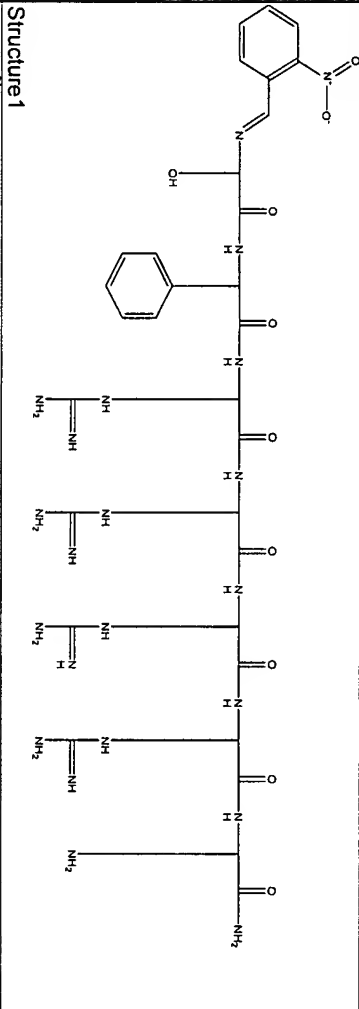
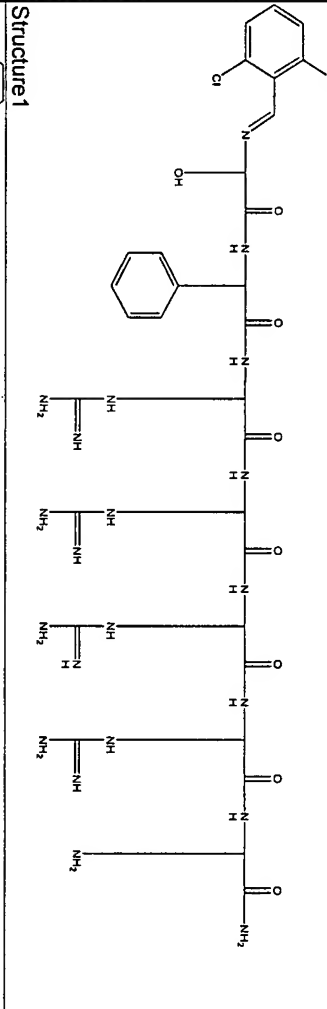
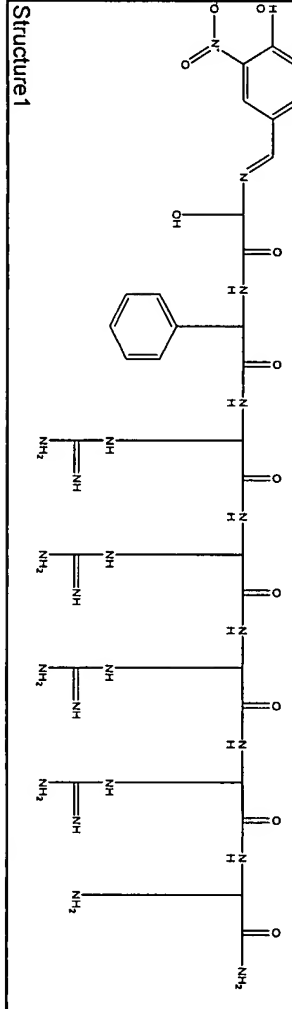
1159.3618	<10%
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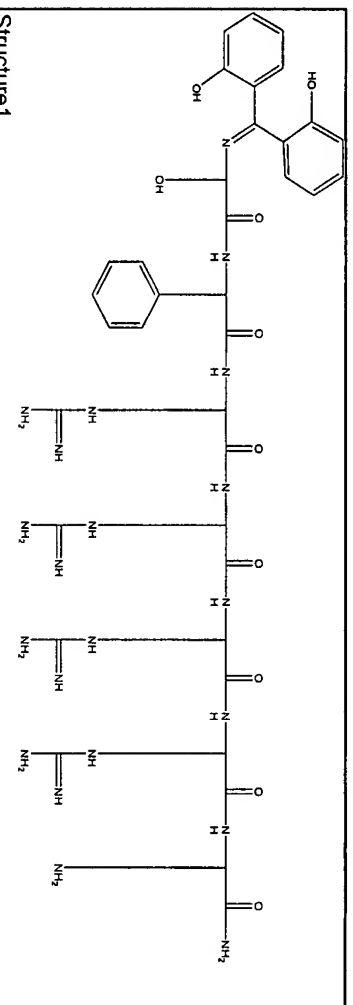
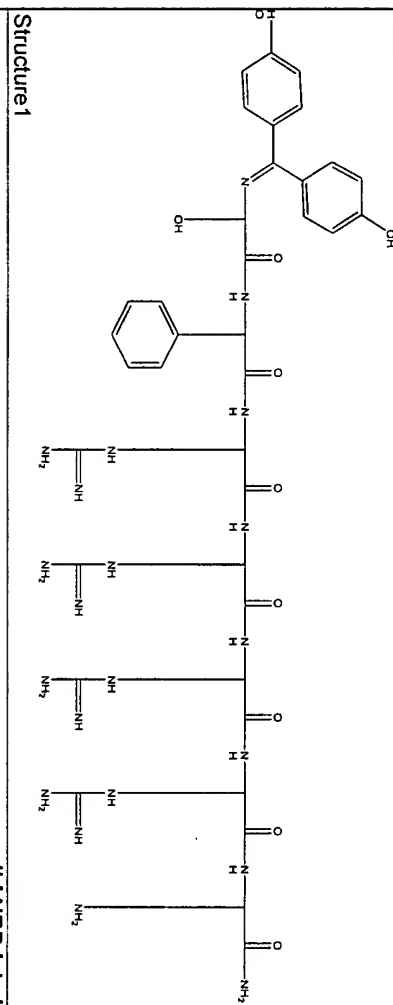
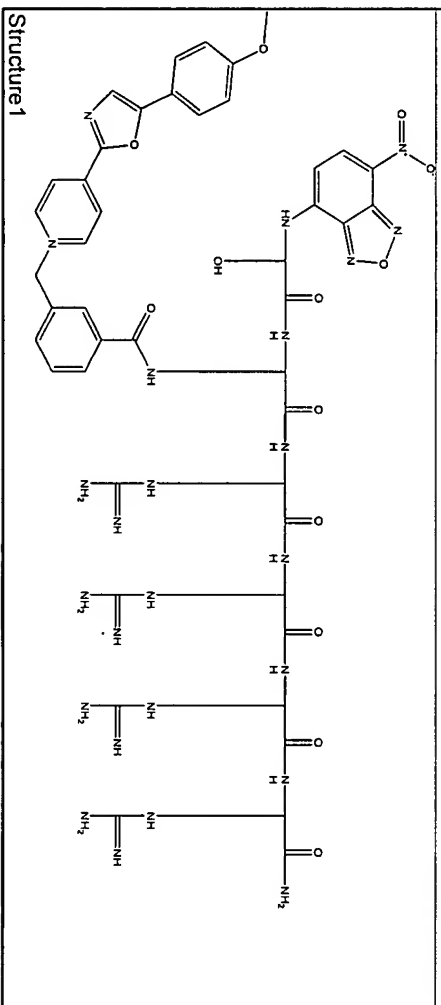
		C66H98N23O10+	1373.6483	<10%
<p>Structure 1</p>				
		C54H88N22O10S	1237.4906	20%
<p>Structure 1</p>				
<p>Imine</p>				
		C53H83N21O9	1158.374	<10%
<p>Structure 1</p>				
		C57H87N21O8	1194.4502	<10%
<p>Structure 1</p>				

<p>Structure 1</p> 	C57H85N21O8	1192.4344	<10%
<p>Structure 1</p> 	C49H79N23O13	1198.3094	<10%
<p>Structure 1</p> 	C51H86N22O9	1151.3824	<10%
<p>Structure 1</p> 	C55H90N22O8	1187.4586	<10%

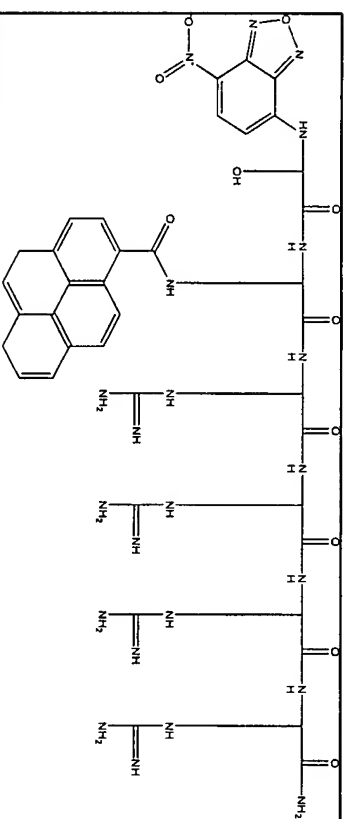
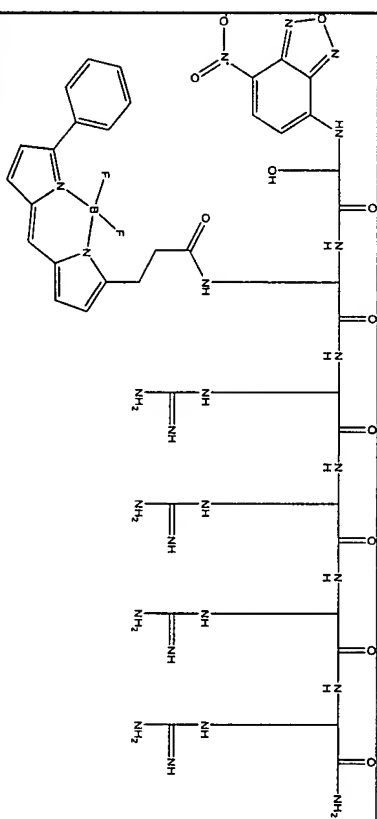
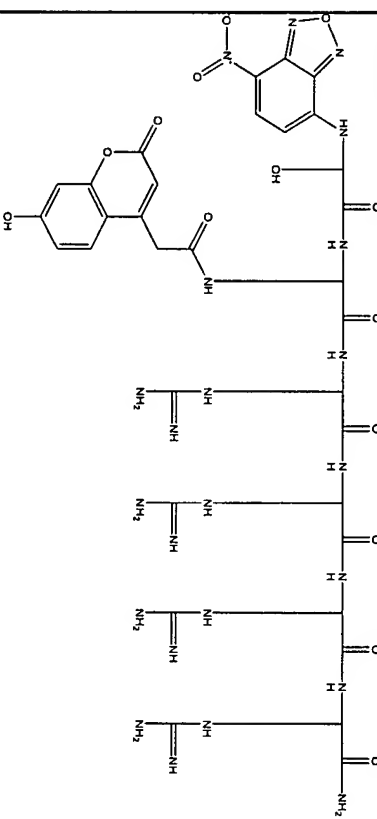
 Structure 1	C53H88N22O8	1161.4208	<10%
 Structure 1	C51H83N21O8	1118.3526	<10%
 Structure 1	C59H87N21O8	1218.4722	<10%
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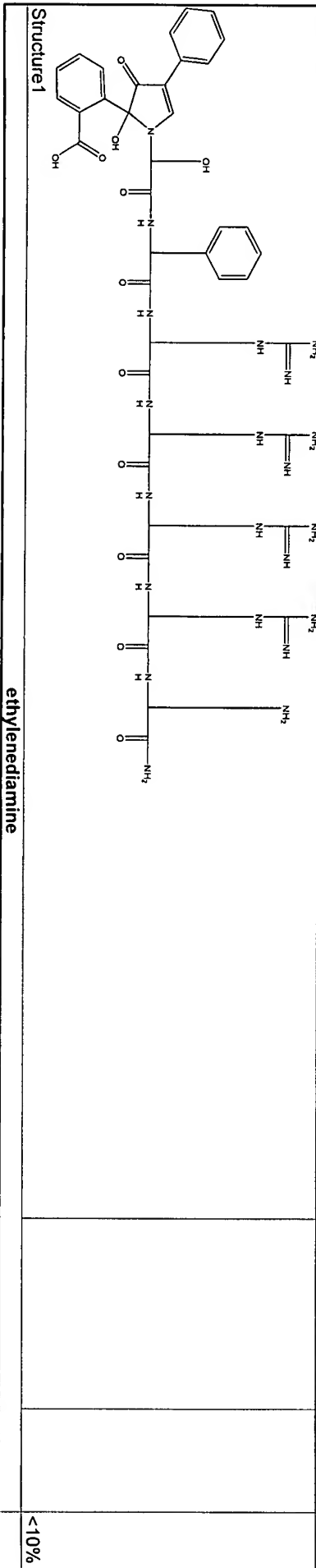
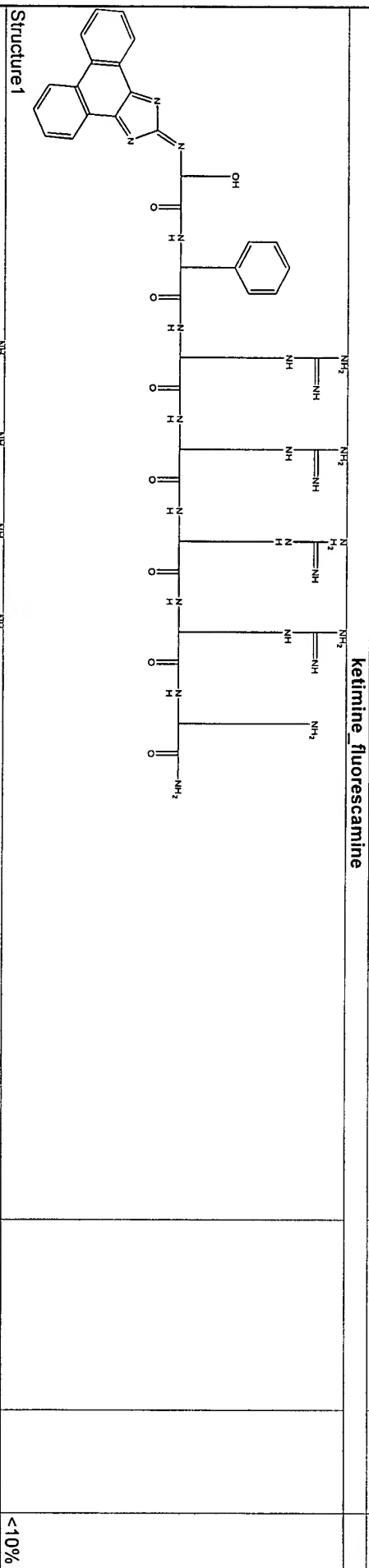
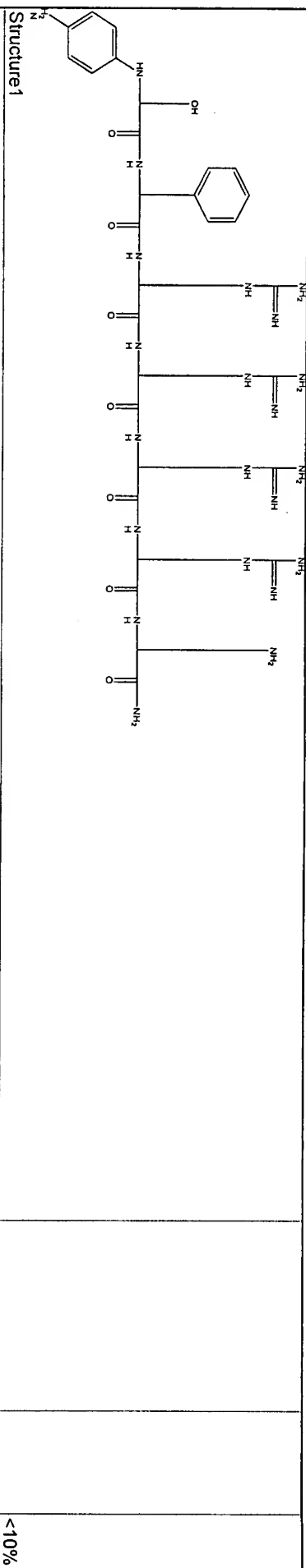
<p>Structure 1</p>  <p>Structure 1</p>	<p>C50H83N21O10</p>	<p>1136.3404</p>	<p><10%</p>
<p>Structure 1</p>  <p>Structure 1</p>	<p>C57H85N21O8</p>	<p>1192.4344</p>	<p><10%</p>
<p>Structure 1</p>  <p>Structure 1</p>	<p>C49H81N21O9</p>	<p>1108.3142</p>	<p><10%</p>
<p>Structure 1</p>  <p>Structure 1</p>	<p>C49H80N22O10</p>	<p>1137.3124</p>	<p><10%</p>

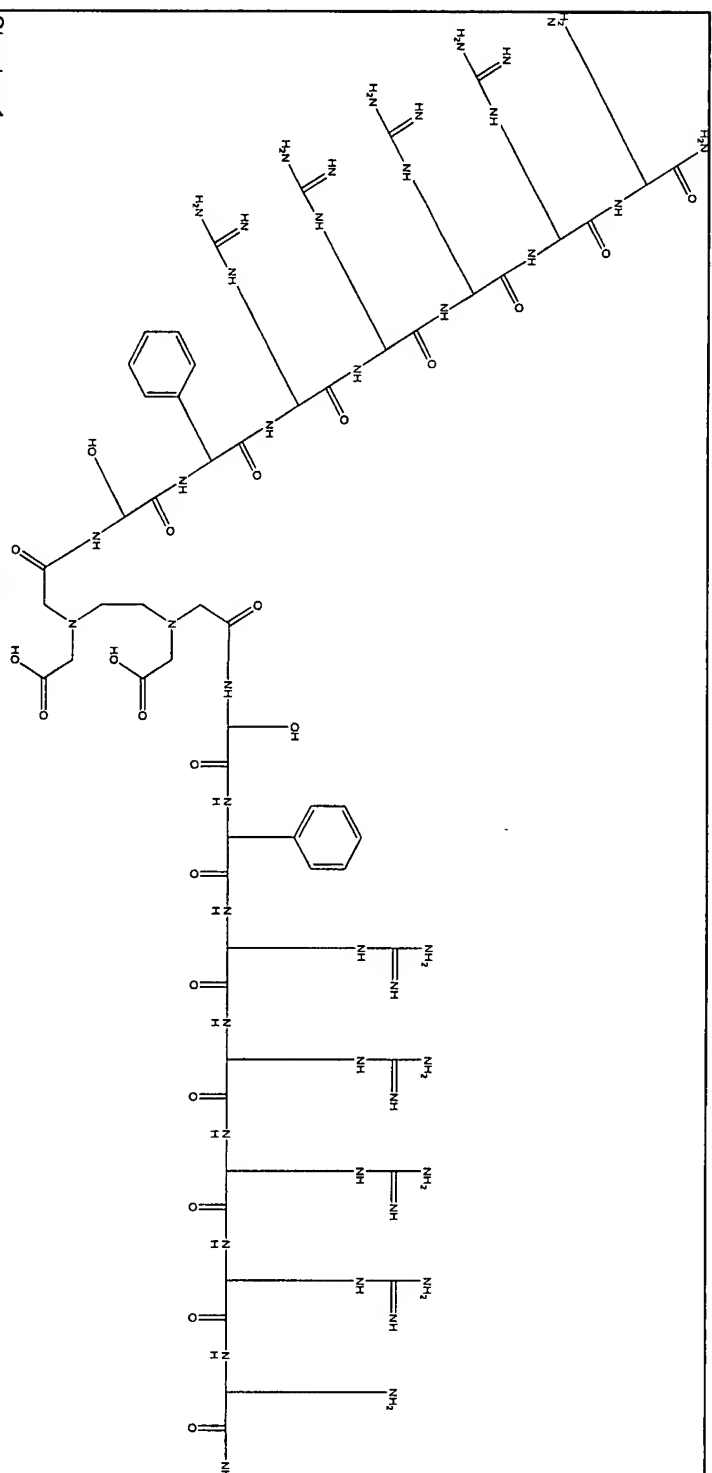
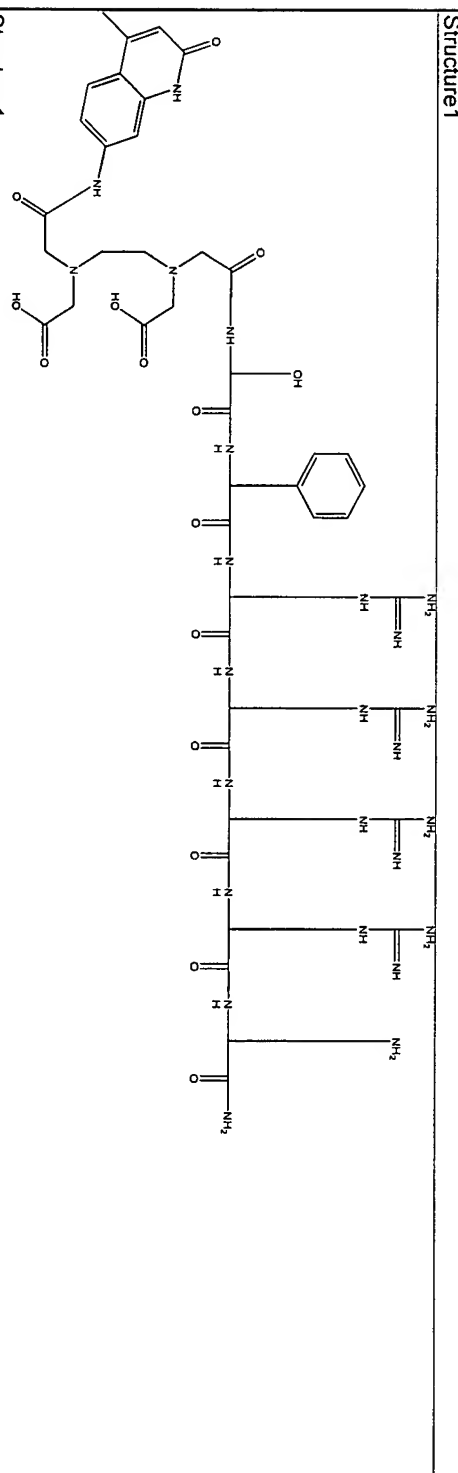
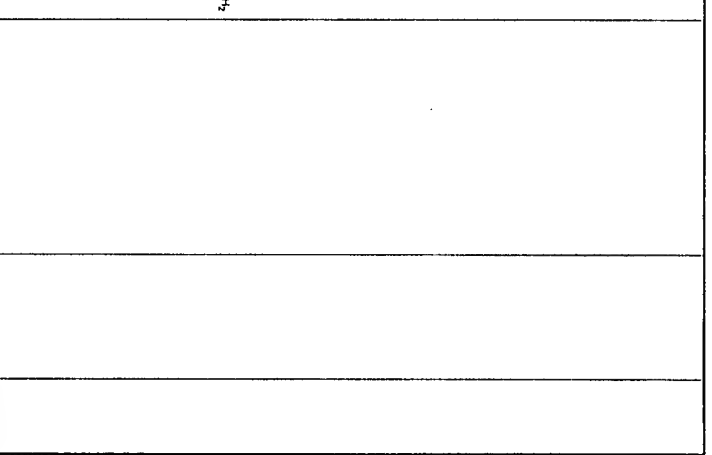
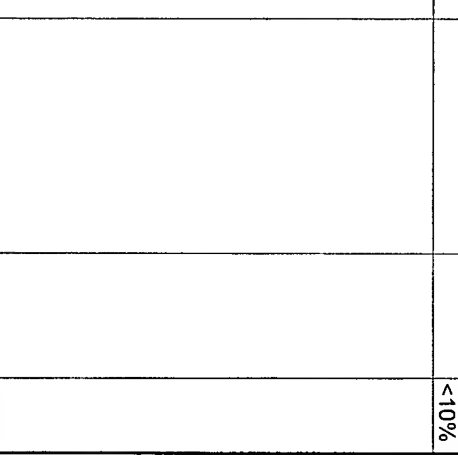
<p>Structure 1</p>  <p>Chemical structure of a peptide derivative. The N-terminus is a 3,4-dimethoxyphenyl group. The peptide backbone consists of 10 residues: Phe, Ser, Arg, Arg, Arg, Arg, Arg, Arg, Arg, and Arg. The C-terminus is an amide group.</p>	C51H85N21O10	1152.3672	<10%
<p>Structure 1</p>  <p>Chemical structure of a peptide derivative. The N-terminus is a 2-chloro-3-(chloromethyl)phenyl group. The peptide backbone consists of 10 residues: Phe, Ser, Arg, Arg, Arg, Arg, Arg, Arg, Arg, and Arg. The C-terminus is an amide group.</p>	C49H80N22O10	1137.3124	<10%
<p>Structure 1</p>  <p>Chemical structure of a peptide derivative. The N-terminus is a 2-chloro-3-(chloromethyl)phenyl group. The peptide backbone consists of 10 residues: Phe, Ser, Arg, Arg, Arg, Arg, Arg, Arg, Arg, and Arg. The C-terminus is an amide group.</p>	C49H79Cl2N21O8	1161.205	<10%
<p>Structure 1</p>  <p>Chemical structure of a peptide derivative. The N-terminus is a 2-chloro-3-(chloromethyl)phenyl group. The peptide backbone consists of 10 residues: Phe, Ser, Arg, Arg, Arg, Arg, Arg, Arg, Arg, and Arg. The C-terminus is an amide group.</p>	C49H80N22O11	1153.3118	<10%

<p>Structure 1</p>  <p>Chemical structure of Structure 1 (top): A long-chain molecule with a central amide backbone. It features a 2,6-dihydroxyphenyl group at one end, a phenyl group in the middle, and a 2,6-dihydroxyphenyl group at the other end. The chain is terminated by amide groups.</p>	C55H85N21O10	1200.4112	<10%
<p>Structure 1</p>  <p>Chemical structure of Structure 1 (middle): A long-chain molecule with a central amide backbone. It features a 2,6-dihydroxyphenyl group at one end, a phenyl group in the middle, and a 2,6-dihydroxyphenyl group at the other end. The chain is terminated by amide groups.</p>	C55H85N21O10	1200.4112	<10%
<p>Structure 1</p>  <p>Chemical structure of Structure 1 (bottom): A long-chain molecule with a central amide backbone. It features a 2,6-dihydroxyphenyl group at one end, a phenyl group in the middle, and a 2,6-dihydroxyphenyl group at the other end. The chain is terminated by amide groups.</p>	C55H85N21O10	1200.4112	<10%

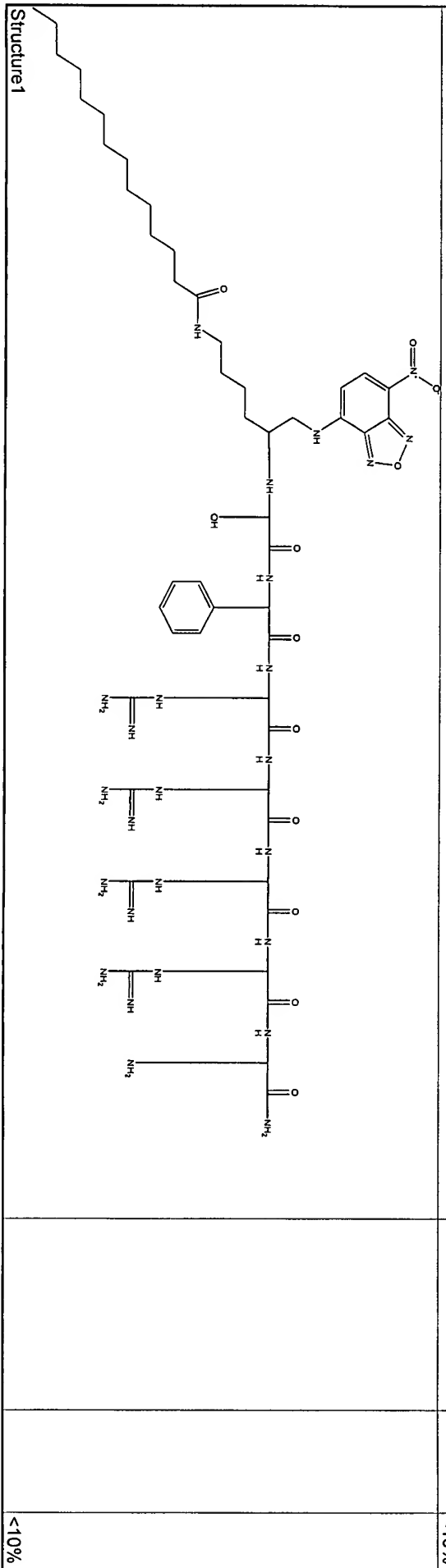
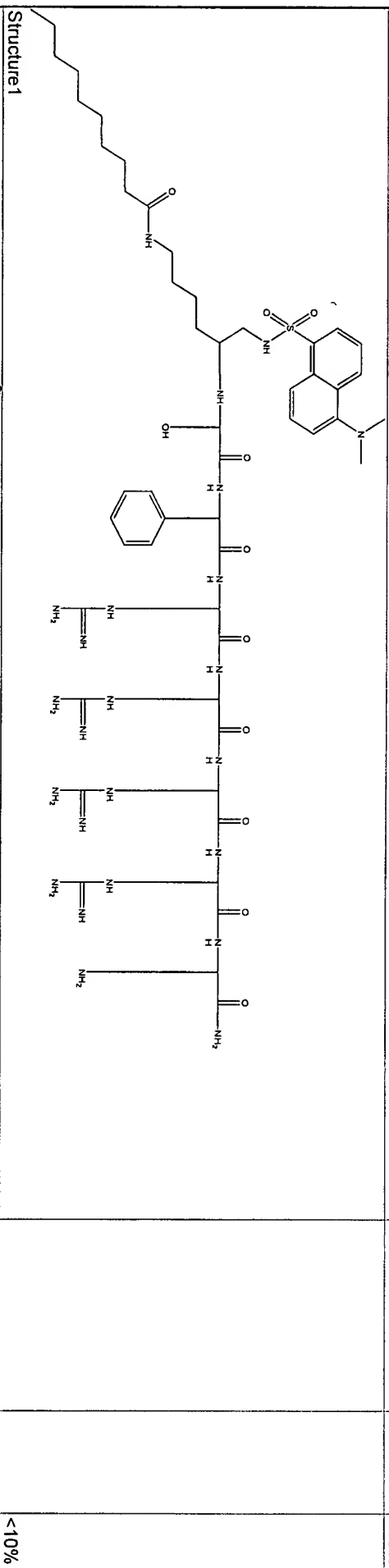
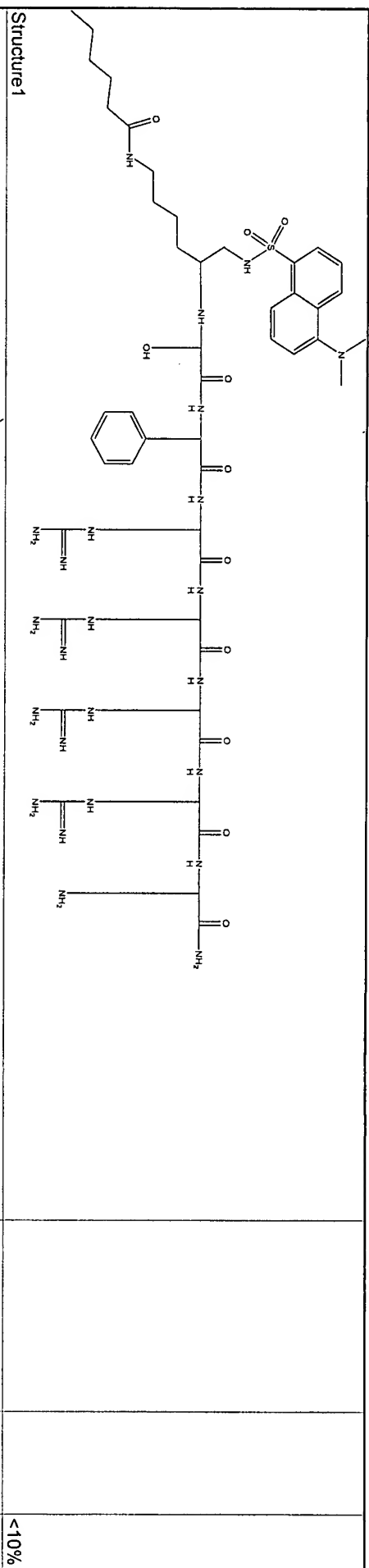
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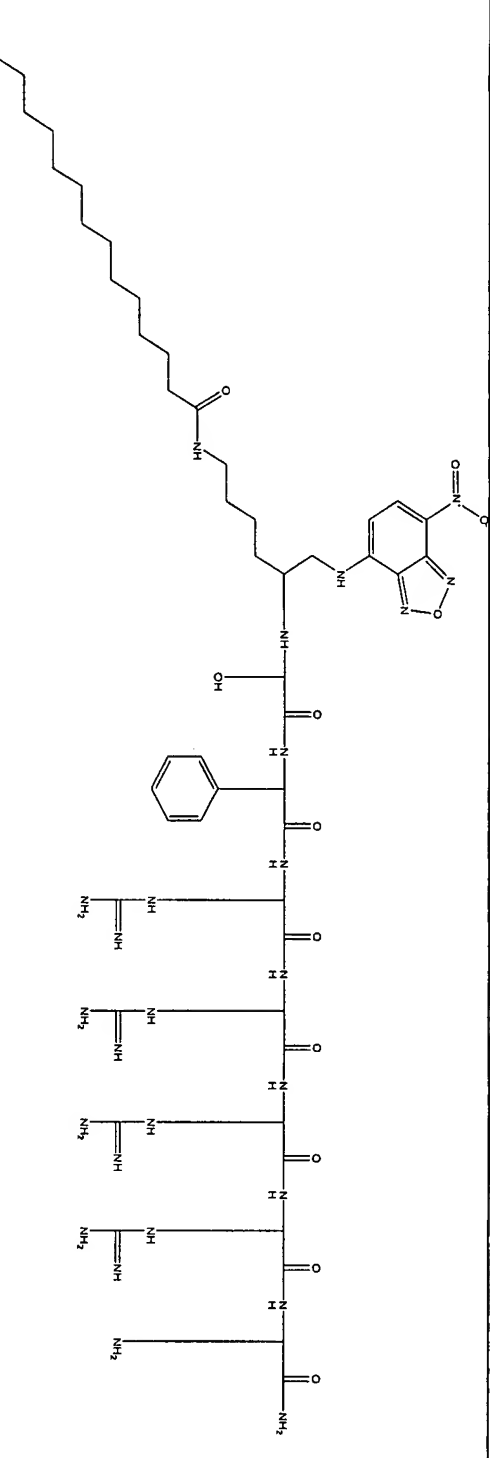
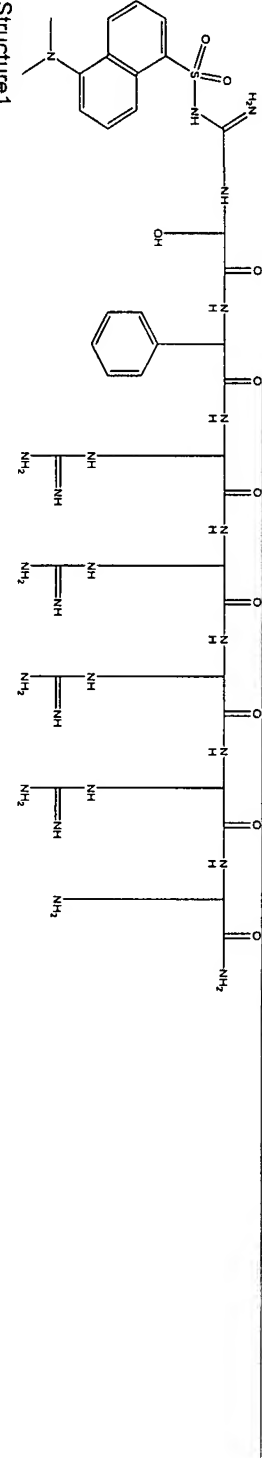
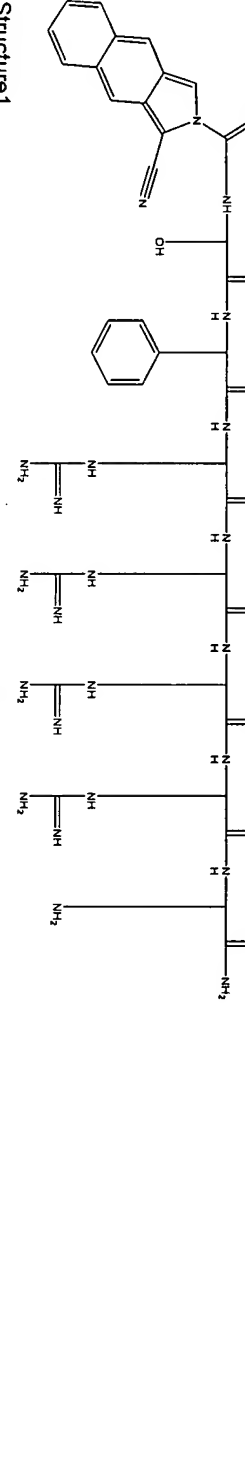
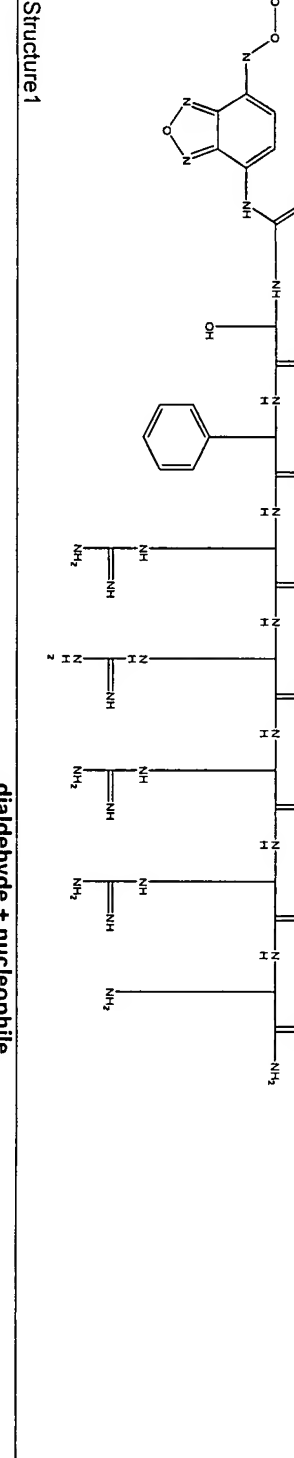
<p>Structure 1</p> 		
<p>Structure 1</p> 		
<p>Structure 1</p> 		
<p>Structure 1</p> <p>Arylation</p>		<p><10%</p>

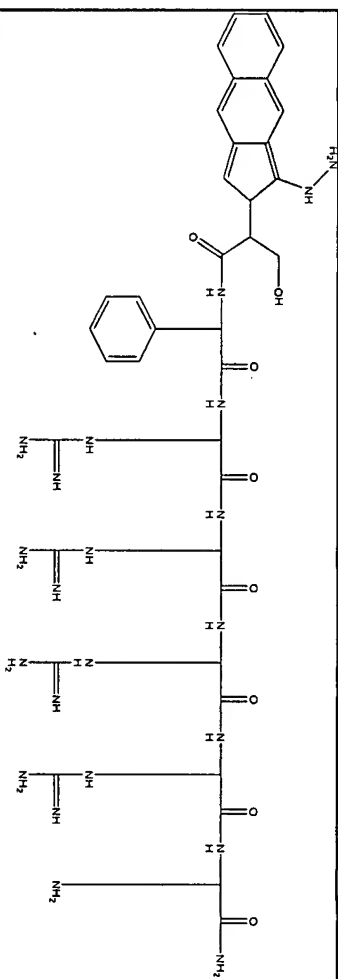


<p>Structure1</p>  <p>Structure1</p> 				<p><10%</p>
<p>Structure1</p>  <p>Structure1</p> 				<p><10%</p>

aminoAla analogs

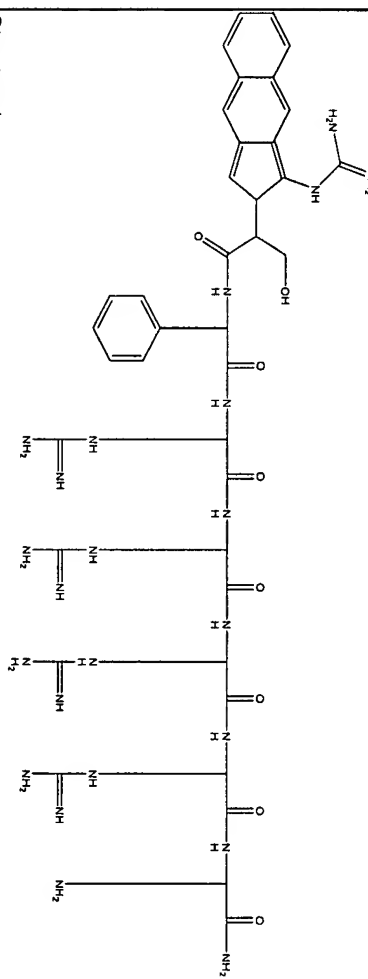


<p>Structure 1</p>  <p>Structure 1</p>	
<p>Structure 1</p> <p>guanidino linkage</p>  <p>Structure 1</p>	
<p>Structure 1</p>  <p>Structure 1</p>	
<p>Structure 1</p>  <p>Structure 1</p>	
<p>dialdehyde + nucleophile</p>	<p><10%</p>



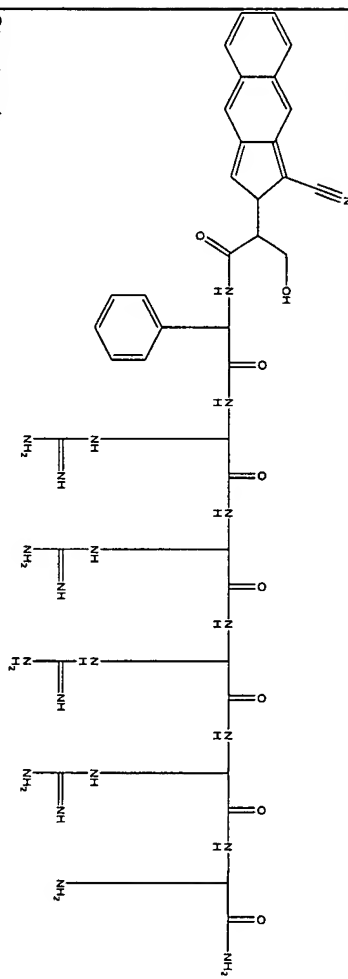
Structure1

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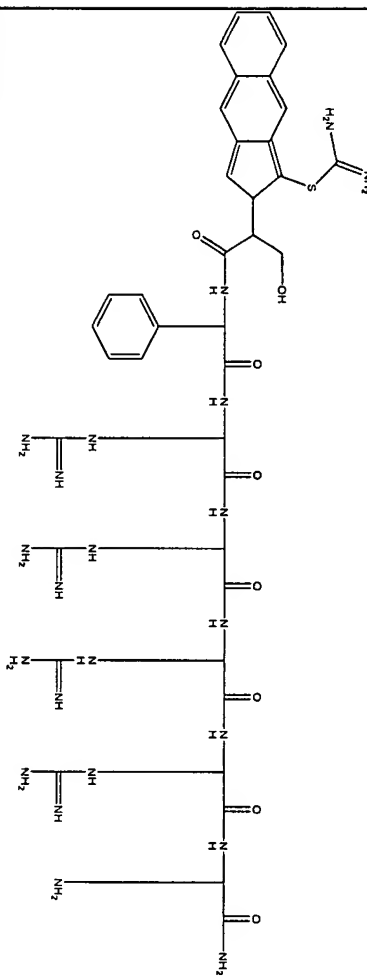
Structure1

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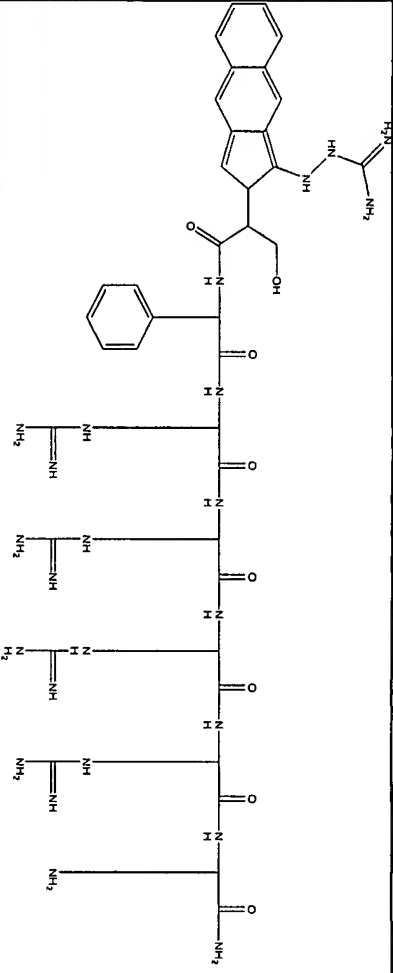
Structure1

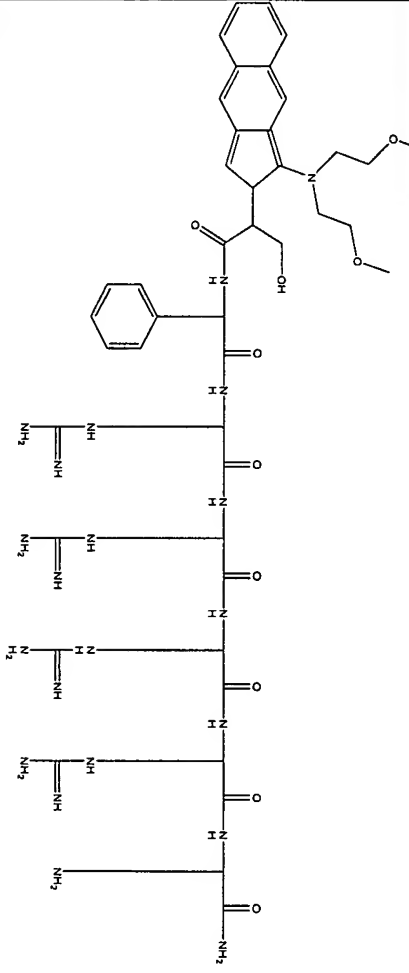
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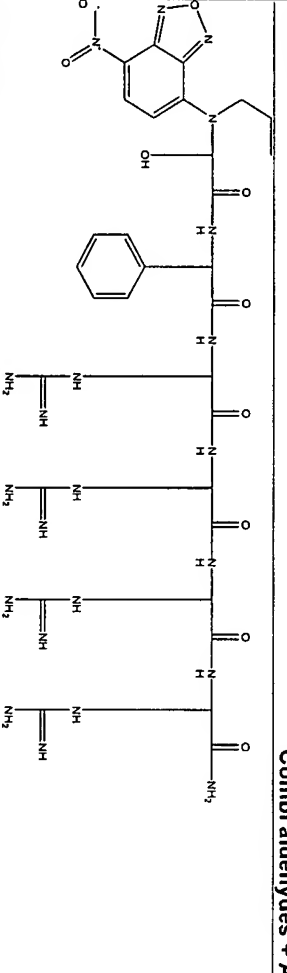


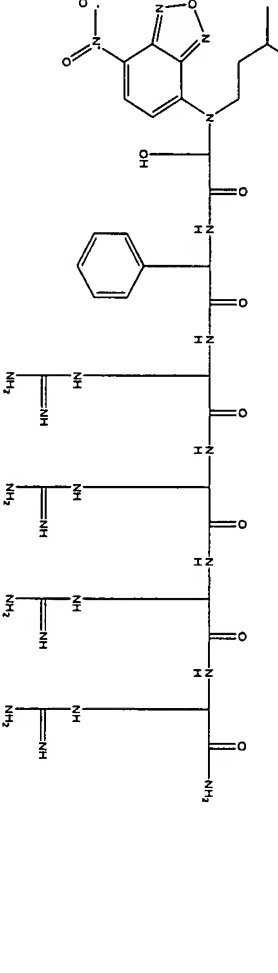
Structure1

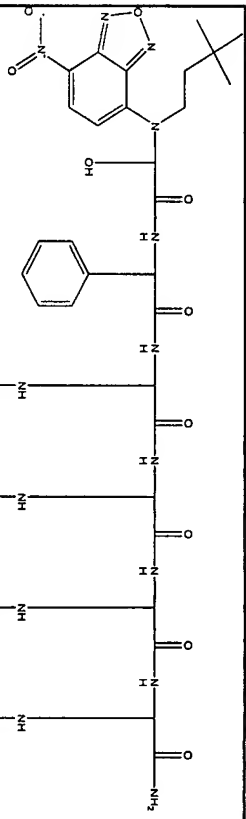
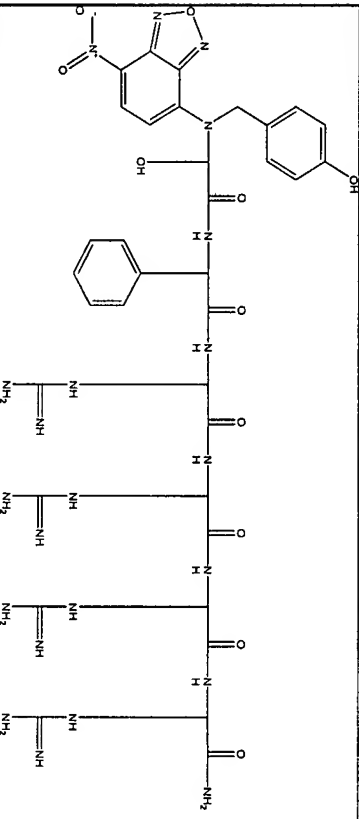
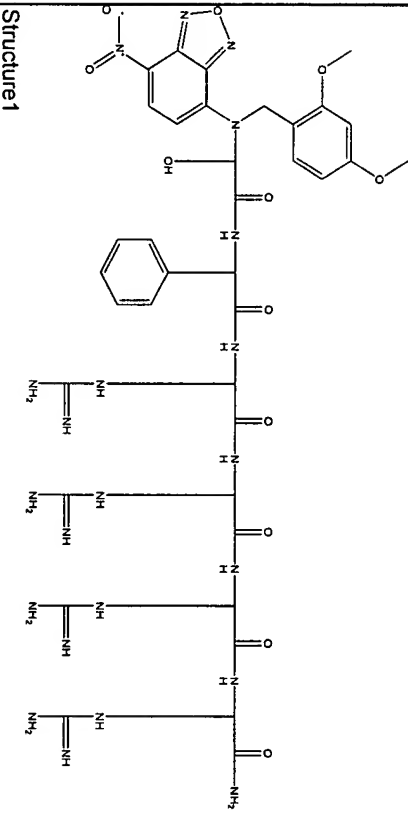
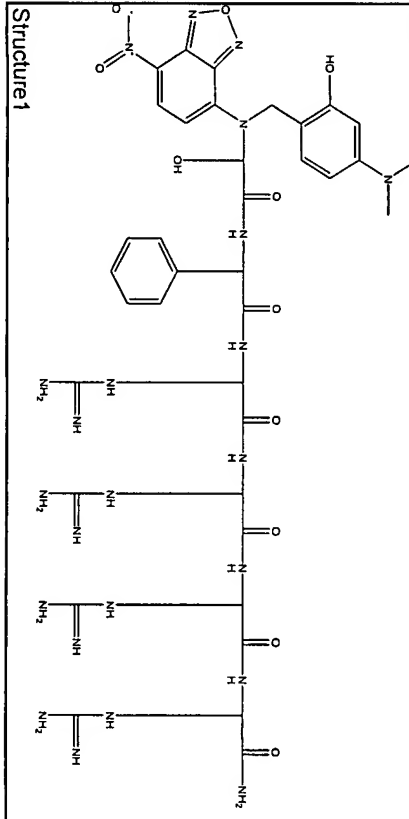
<10%

			
Structure 1			<10%

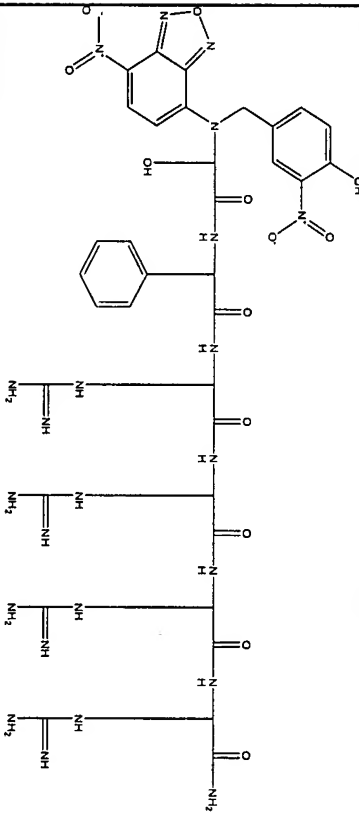
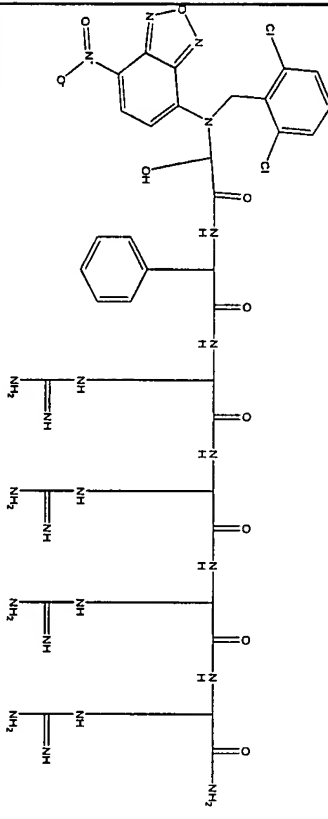
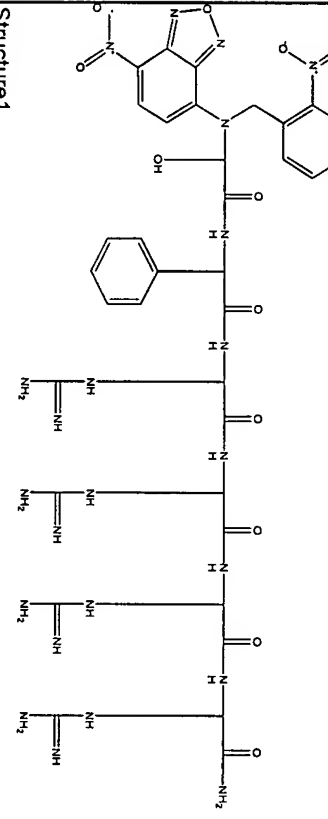
			
Structure 1			<10%

			
Structure 1	C45H72N22O10	1081.2052	<10%

			
Structure 1	C47H76N22O10	1109.2588	<10%

<p>Structure 1</p>  <p>C48H78N22O10</p> <p>1123, 2856 <10%</p>	
<p>Structure 1</p>  <p>C49H72N22O11</p> <p>1145, 2486 <10%</p>	
<p>Structure 1</p>  <p>C51H76N22O12</p> <p>1189, 3016 <10%</p>	
<p>Structure 1</p>  <p>C51H77N23O11</p> <p>1188, 3168 <10%</p>	

<p>Structure1</p> <p>C51H77N23O10</p> <p>1172.3174 <10%</p>
<p>Structure1</p> <p>C49H73N23O12</p> <p>1176.2626 <10%</p>
<p>Structure1</p> <p>C49H71N23O12</p> <p>1174.2468 <10%</p>

<p>Structure 1</p> 			
<p>Structure 1</p> 			
<p>Structure 1</p> 			

C49H71N23O13

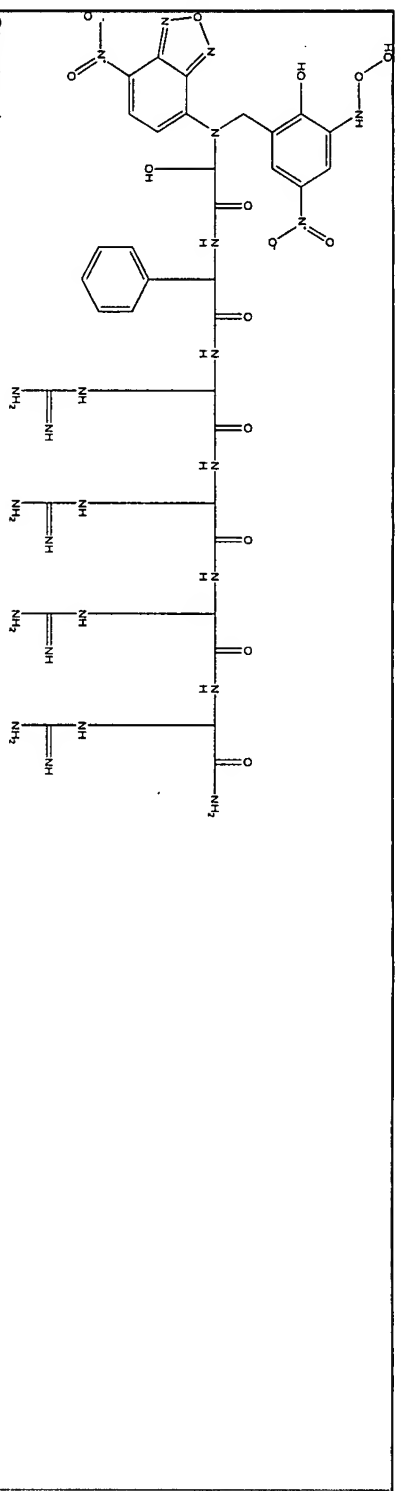
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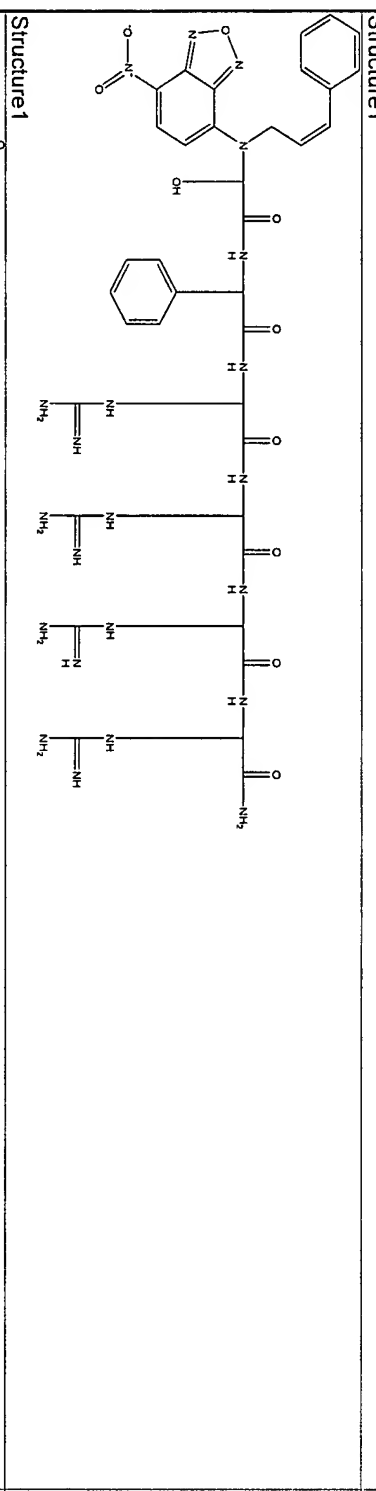
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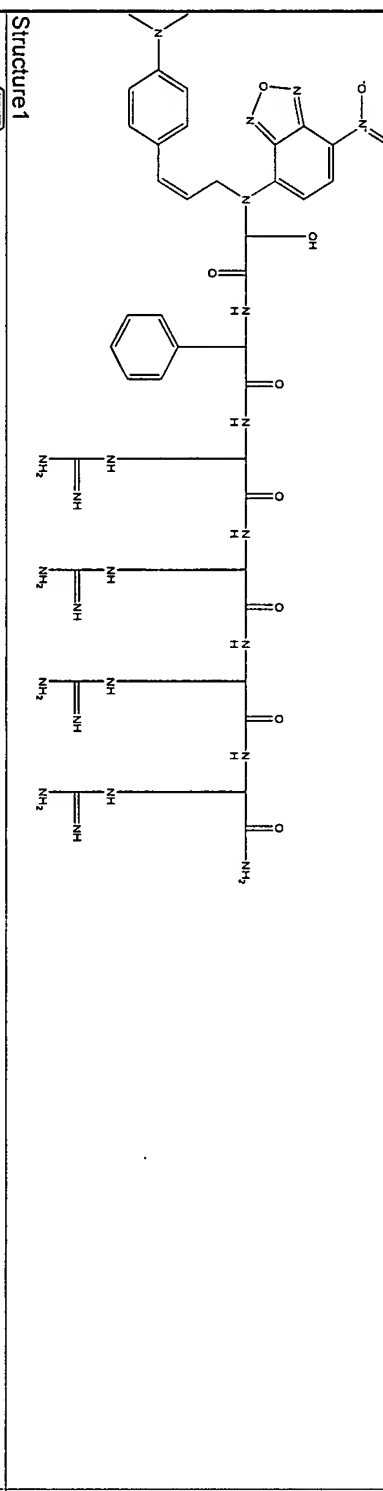
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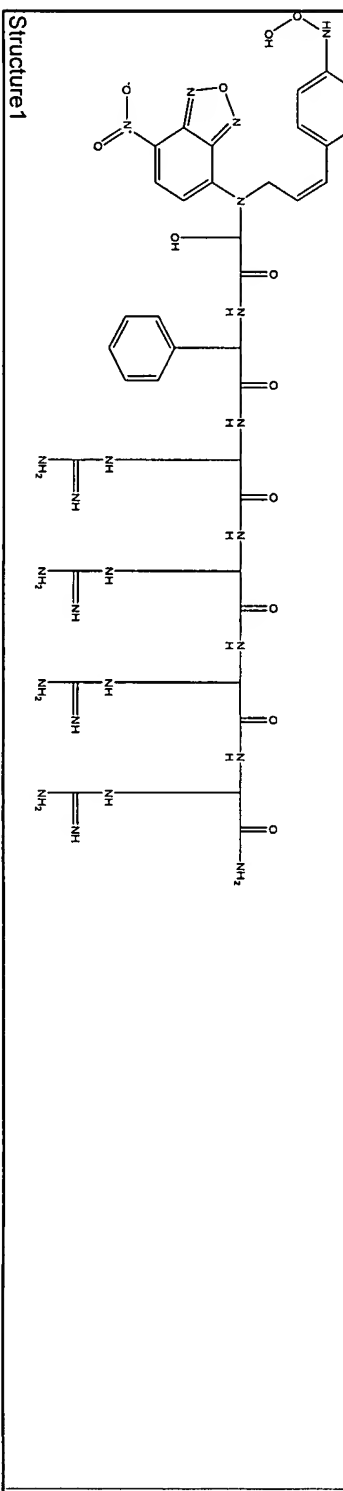
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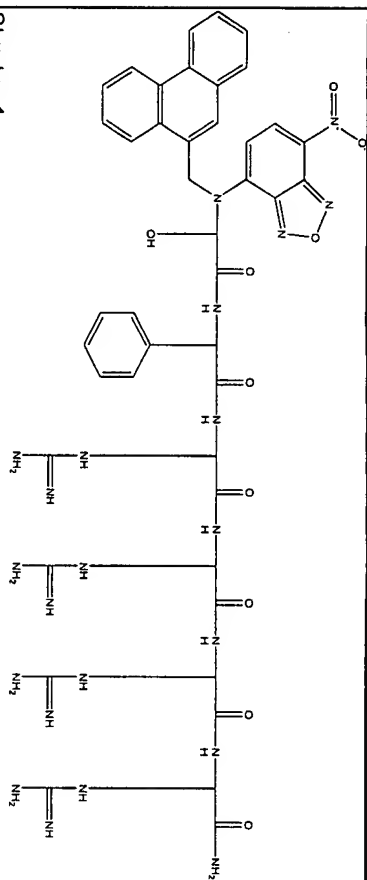
1221.2602 <10%

	C49H72N24O15	1237.2596	<10%
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	C51H74N22O10	1155.287	<10%
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	C53H79N23O10	1198.3552	<10%
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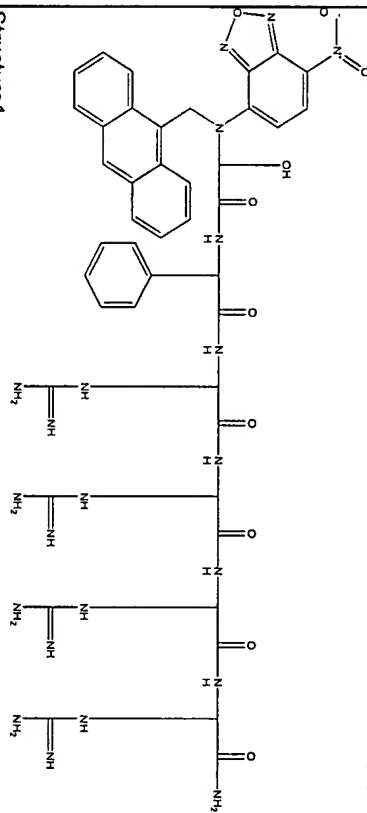
	C51H75N23O12	1202.3004	<10%
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Structure1

C57H76N22O10

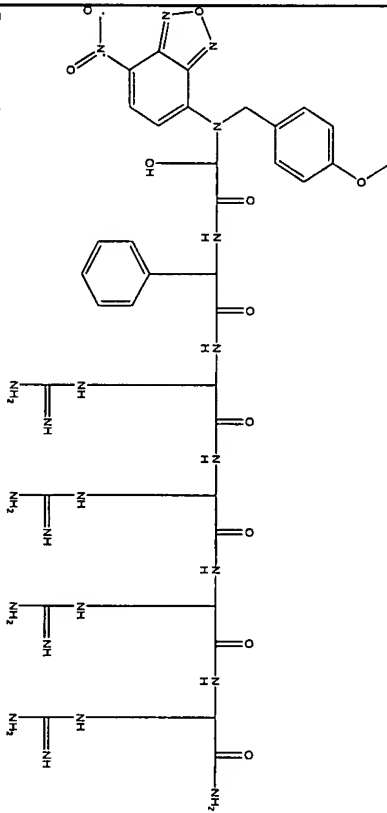
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Structure1

C57H76N22O10

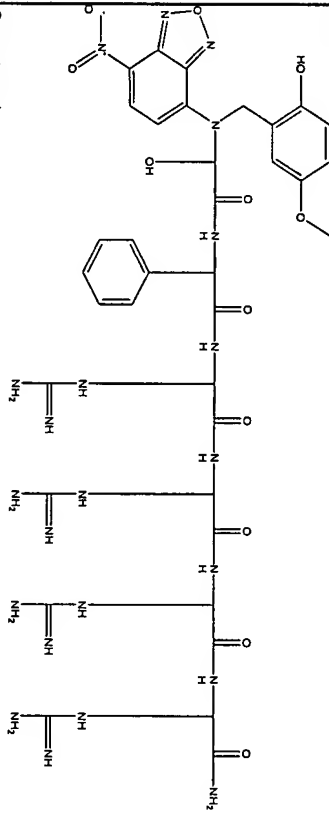
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Structure1

C50H74N22O11

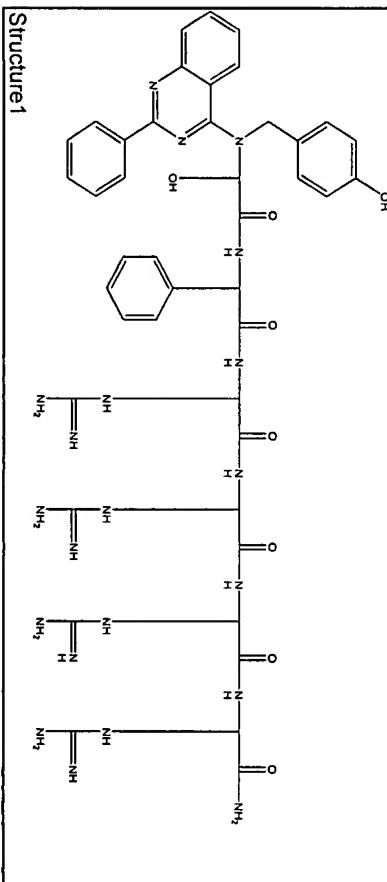
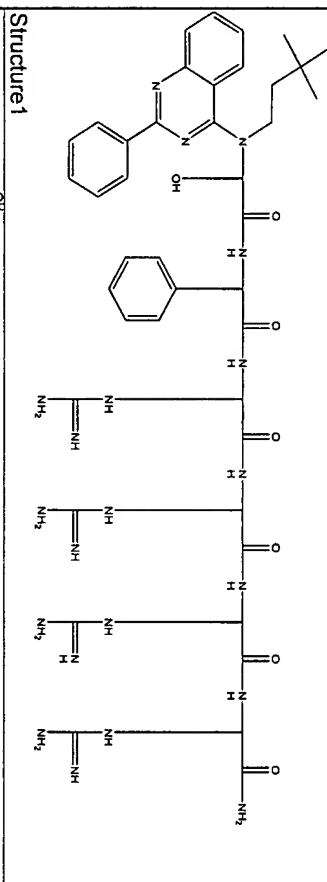
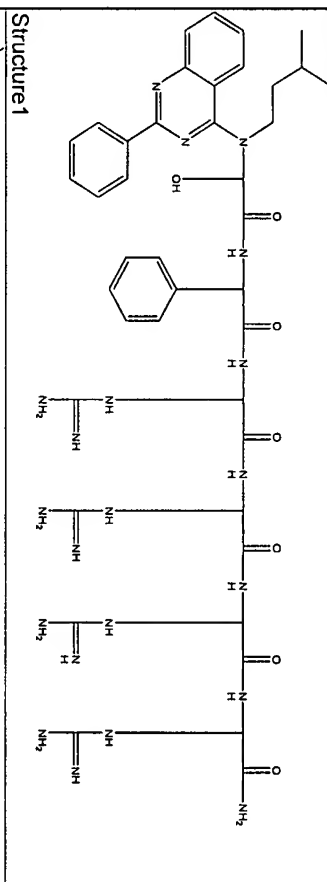
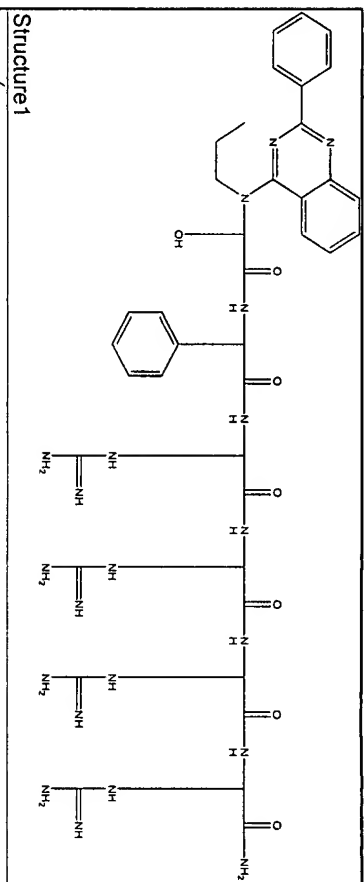
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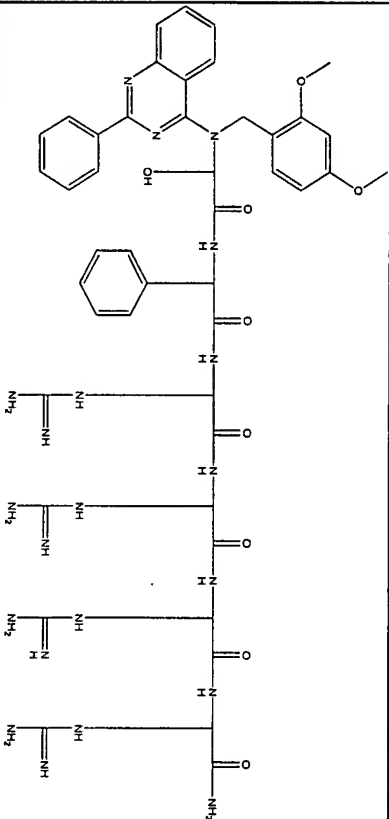
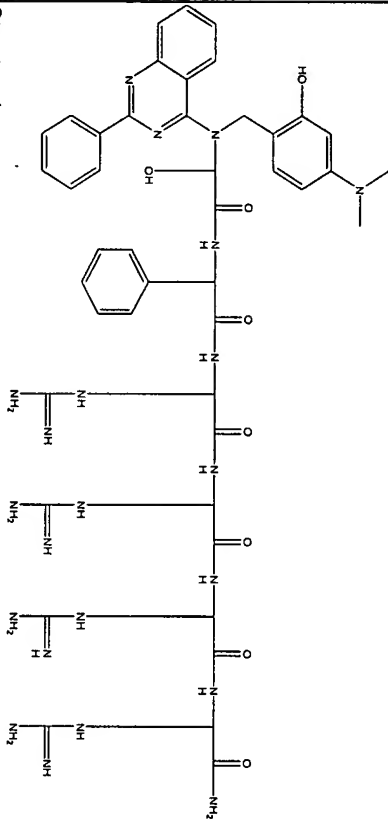
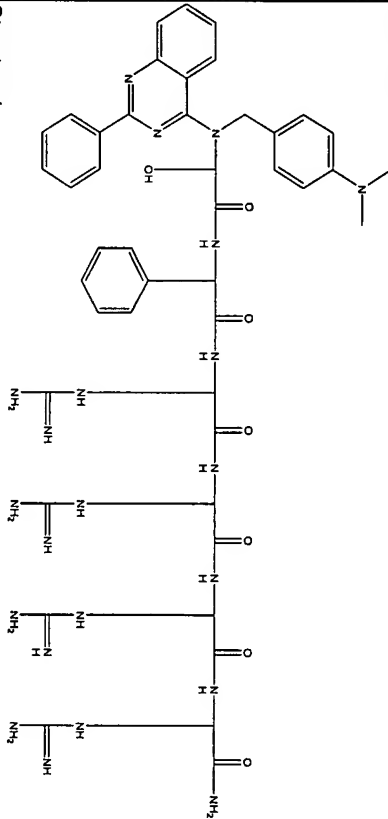


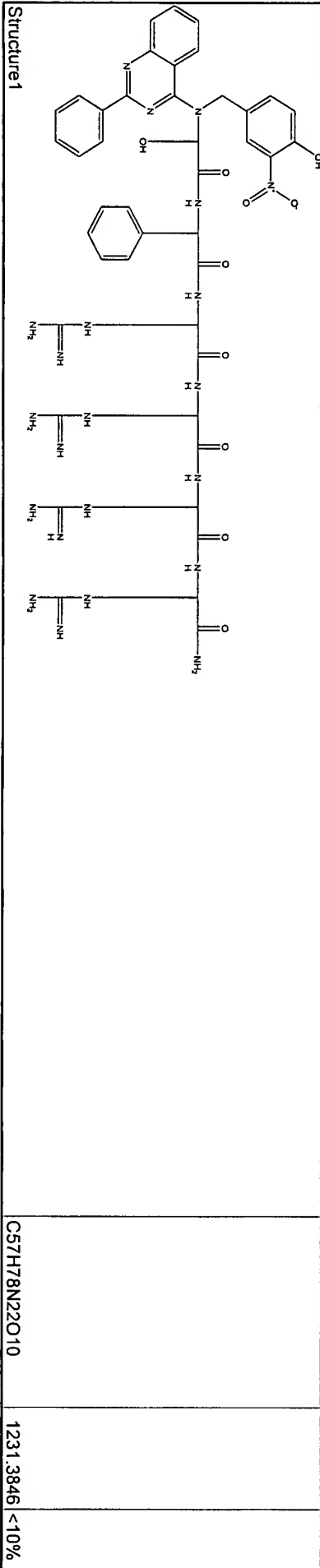
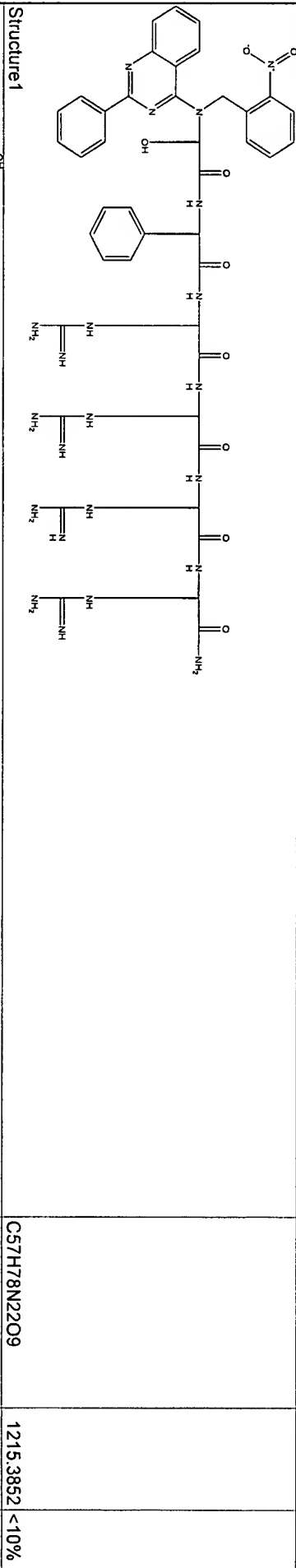
Structure1

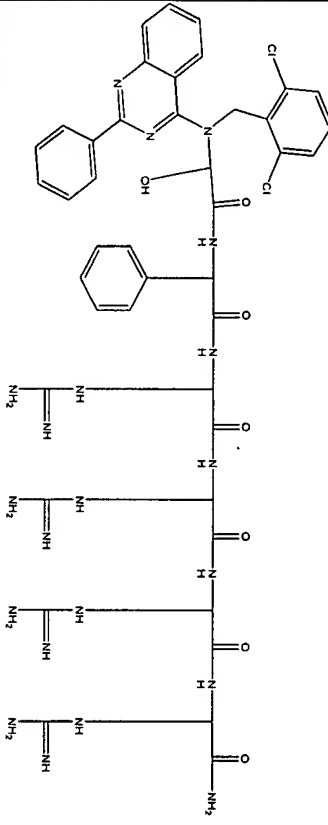
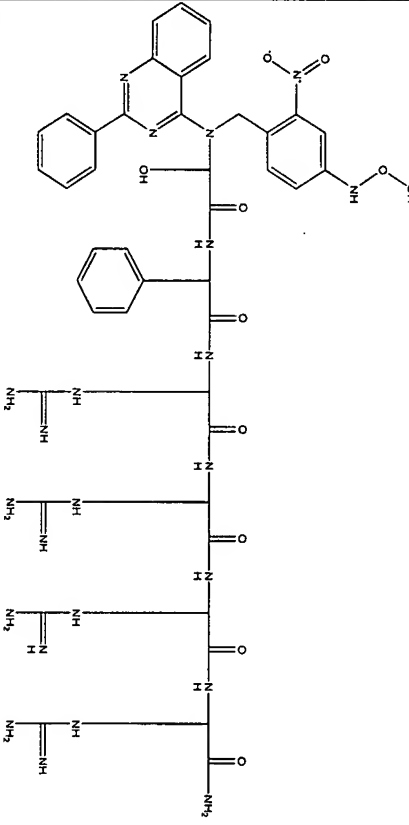
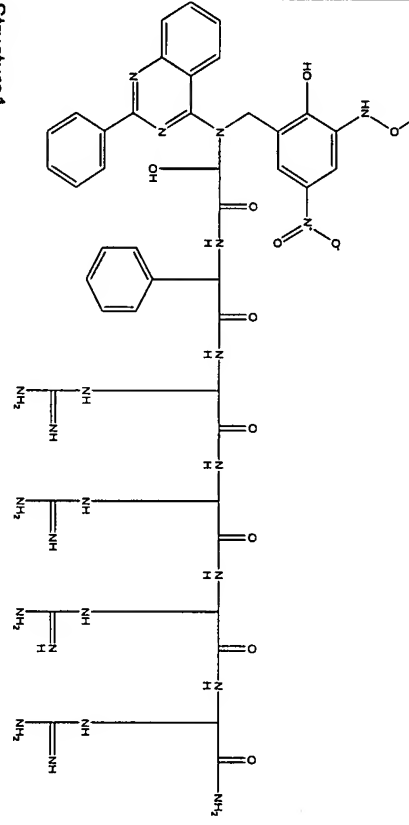
C50H74N22O12

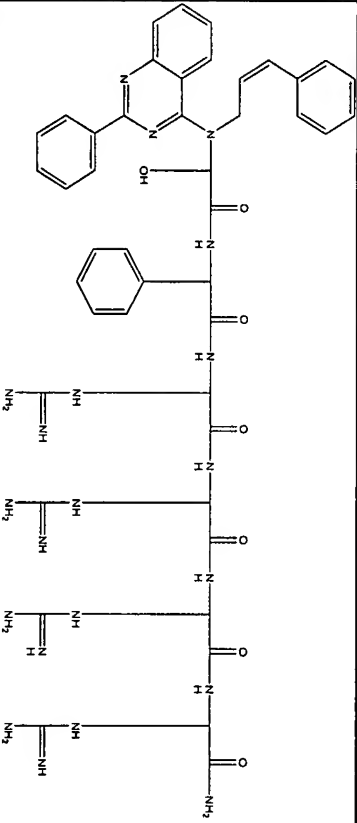
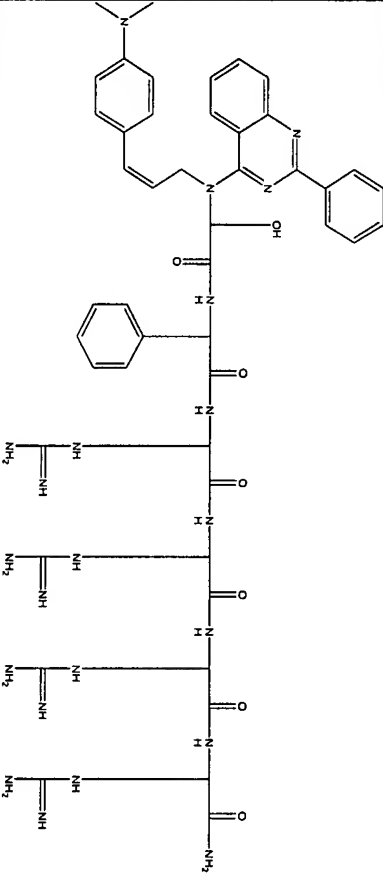
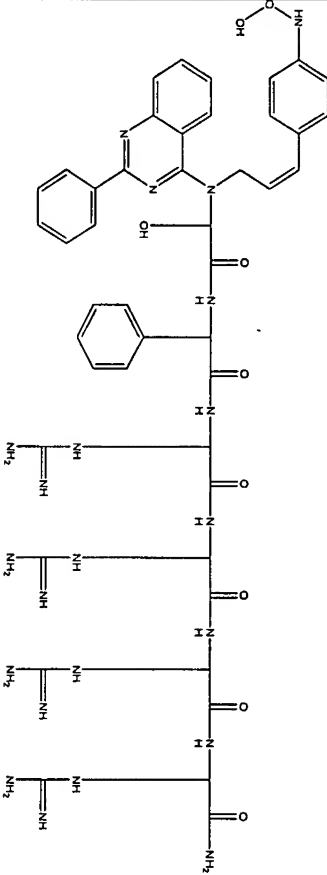
1175.2748 <10%

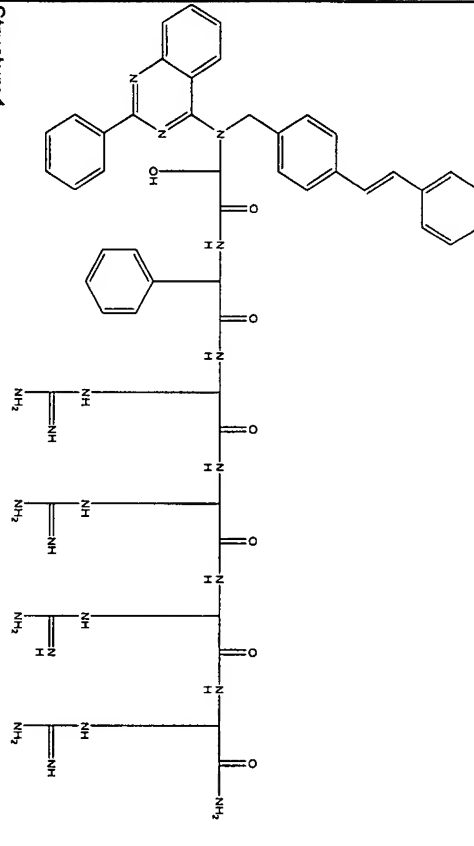
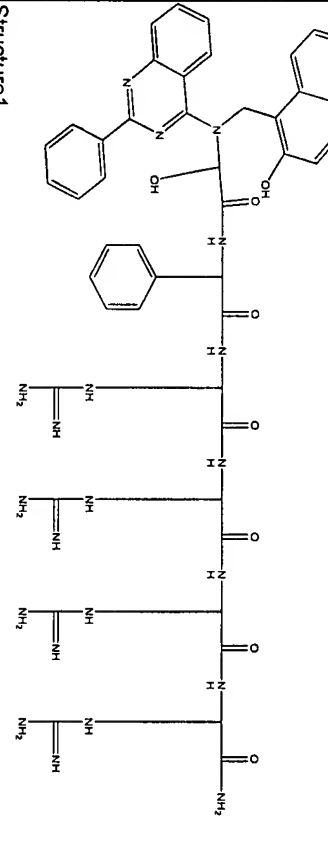
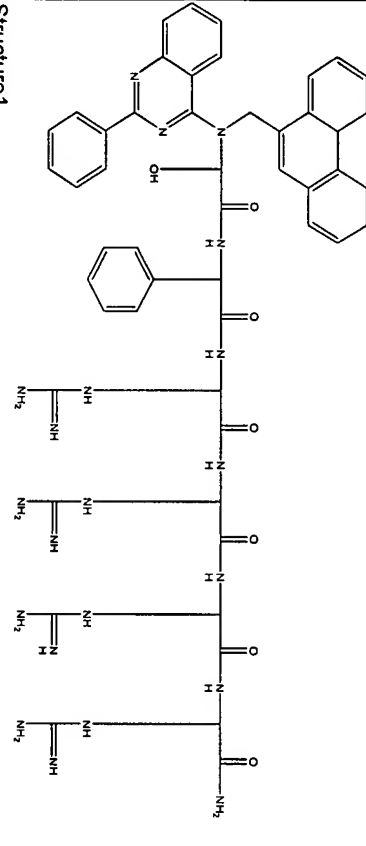
<p>Structure 1</p>  <p>Structure 1</p>	C57H79N21O8	1186.387	<10%
<p>Structure 1</p>  <p>Structure 1</p>	C56H85N21O7	1164.424	<10%
<p>Structure 1</p>  <p>Structure 1</p>	C55H83N21O7	1150.3972	<10%
<p>Structure 1</p>  <p>Structure 1</p>	C53H79N21O7	1122.3436	<10%

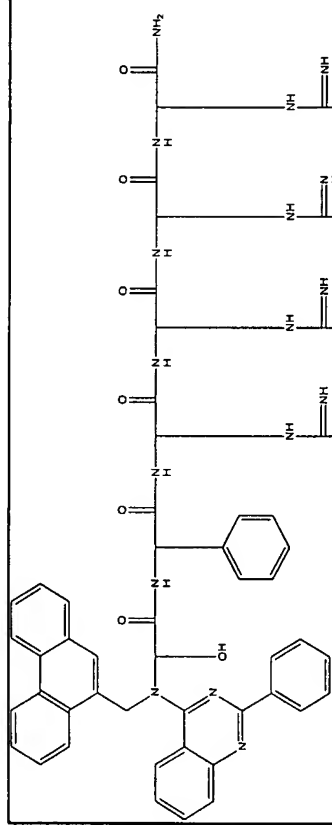
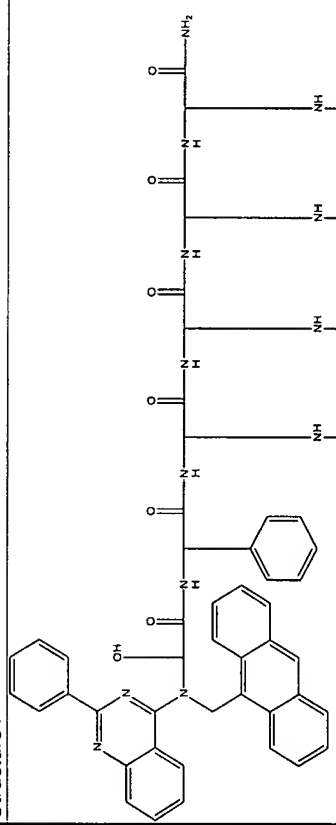
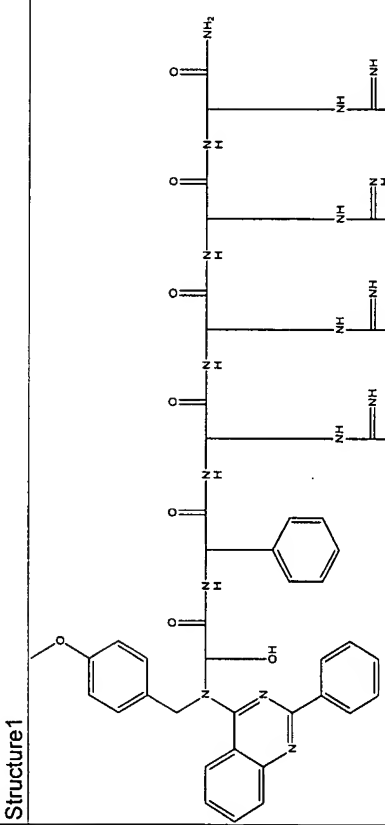
<p>Structure1</p>  <p>C59H83N21O9</p> <p>1230.44</p> <p><10%</p>
<p>Structure1</p>  <p>C59H84N22O8</p> <p>1229.4552</p> <p><10%</p>
<p>Structure1</p>  <p>C59H84N22O7</p> <p>1213.4558</p> <p><10%</p>

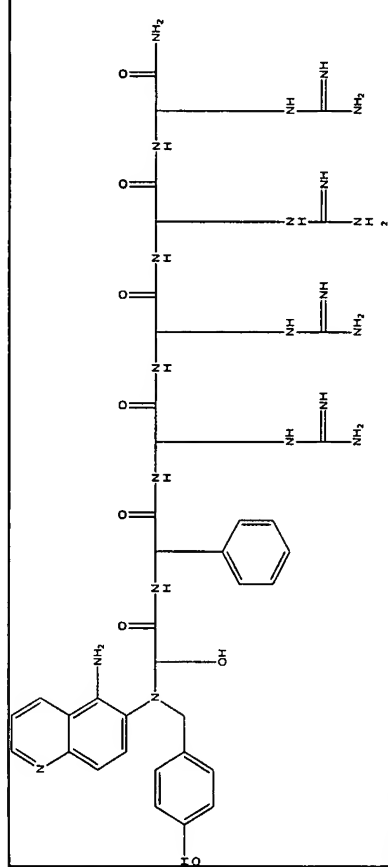
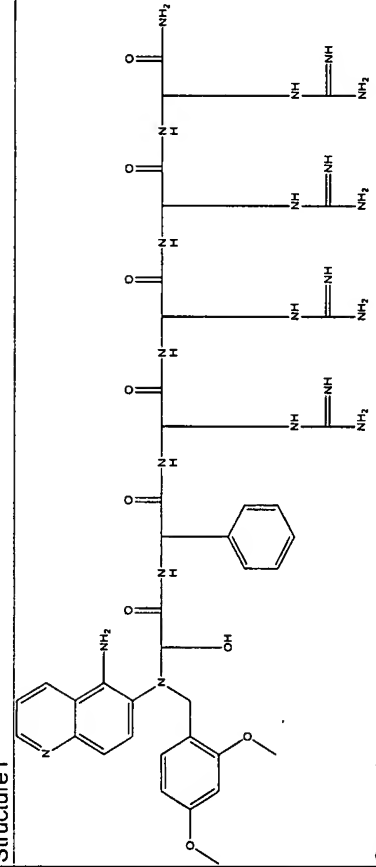
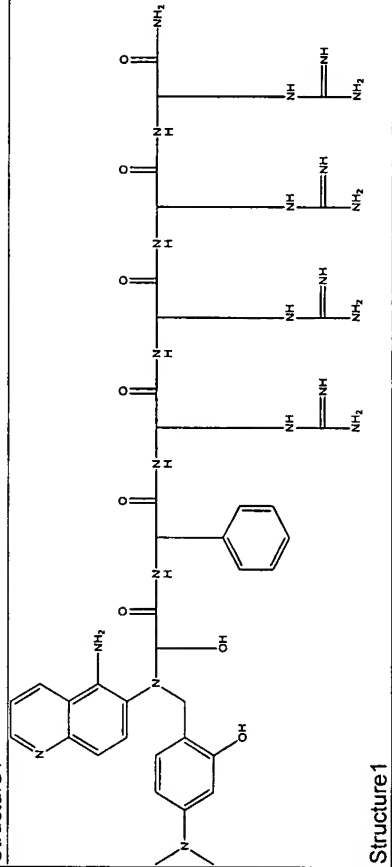


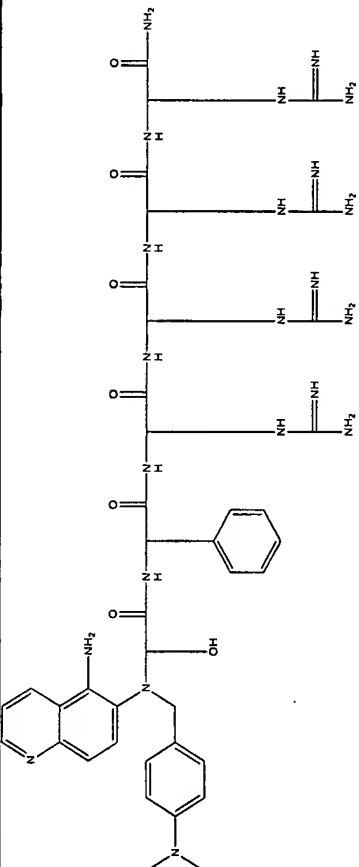
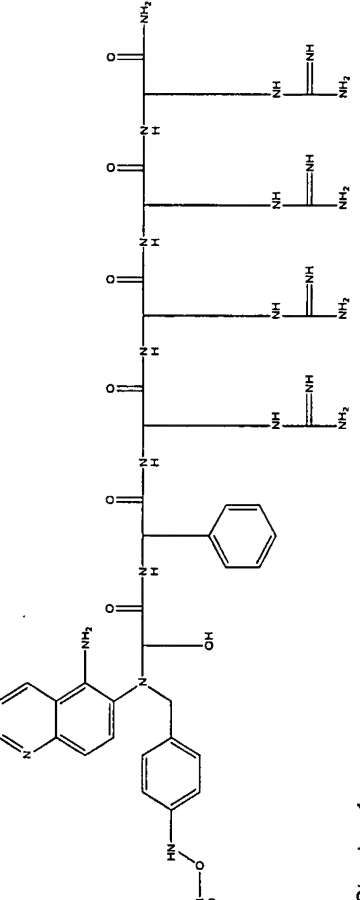
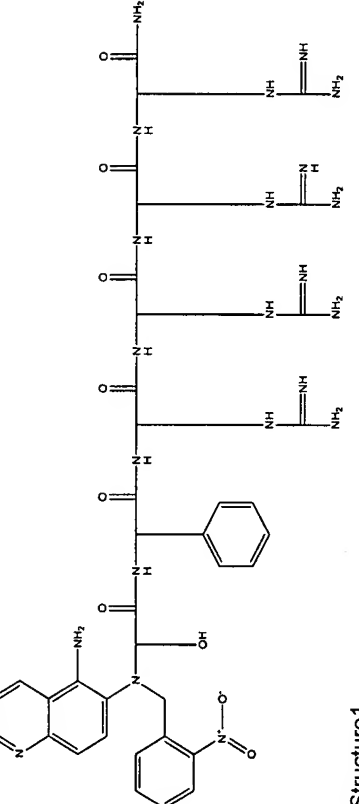
<p>Structure 1</p> 	C57H77Cl2N21O7	1239.2778	<10%
<p>Structure 1</p> 	C57H79N23O11	1262.3986	<10%
<p>Structure 1</p> 	C57H79N23O12	1278.398	<10%

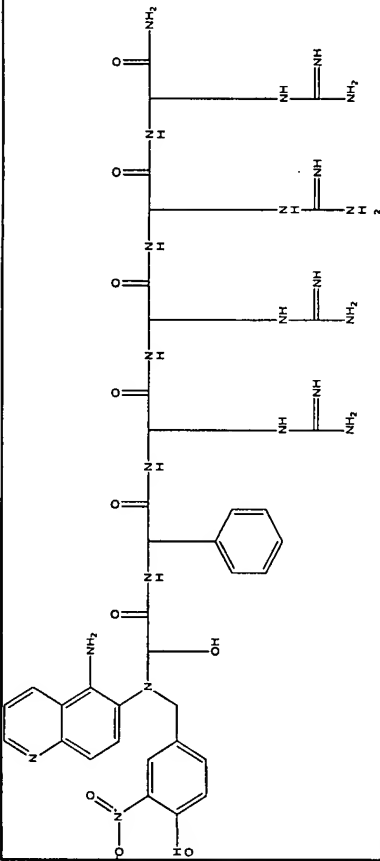
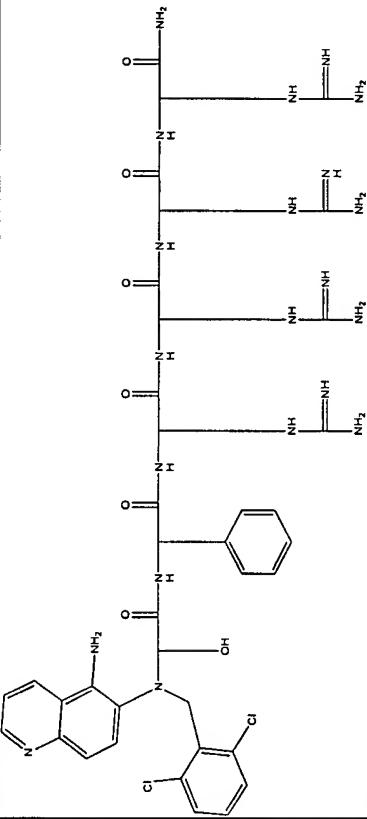
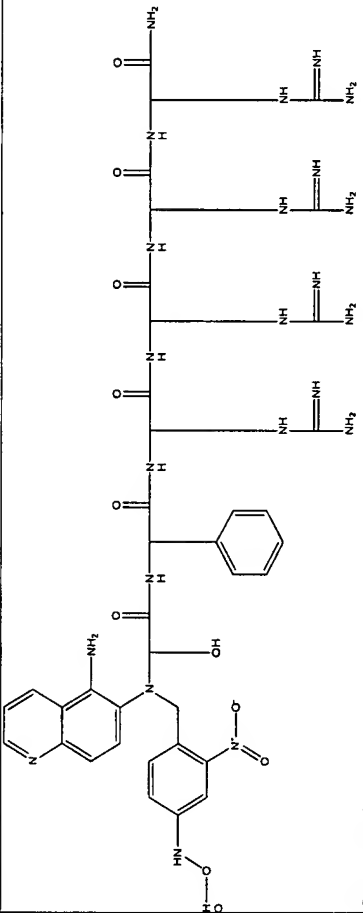
<p>Structure1</p> 		<p>C59H81N21O7</p> <p>1196.4254 <10%</p>
<p>Structure1</p> 		<p>C61H86N22O7</p> <p>1239.4936 <10%</p>
<p>Structure1</p> 		<p>C59H82N22O9</p> <p>1243.4388 <10%</p>

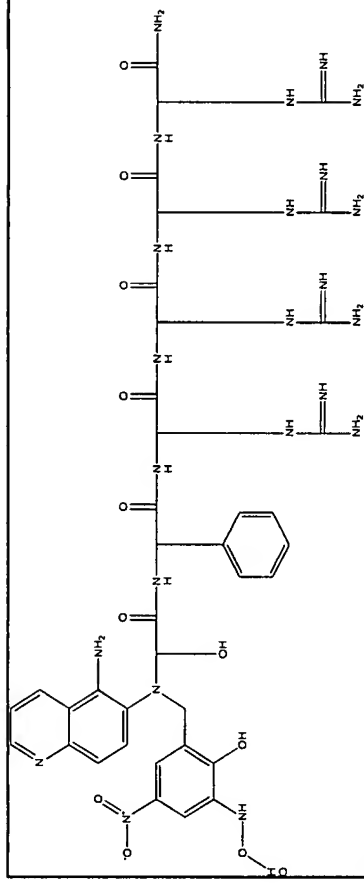
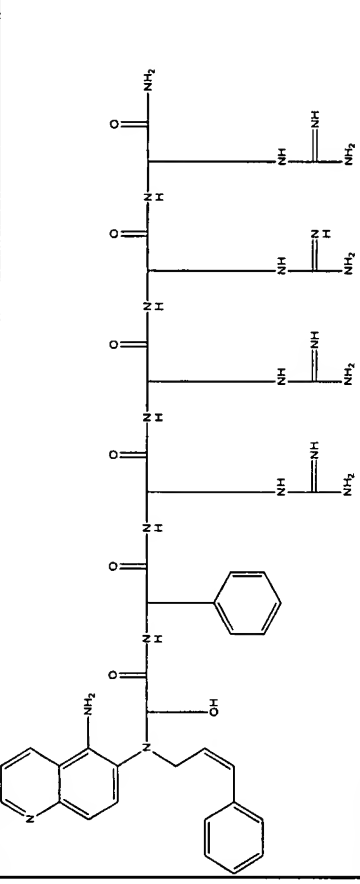
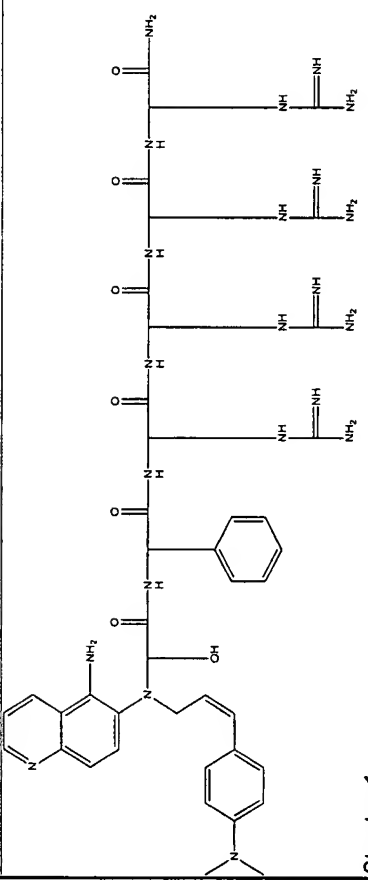
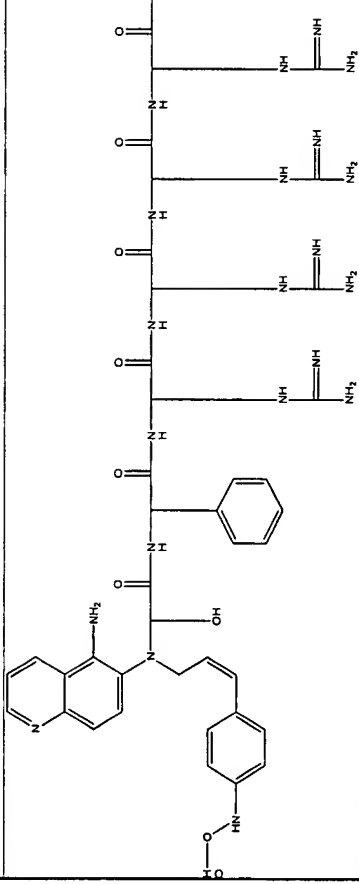
<p>Structure 1</p>  <p>Chemical structure of a protein derivative with a trans-stilbene modification. The structure shows a protein backbone with various side chains, including a 2-phenyl-1H-imidazole-5-ylmethyl group, a 4-hydroxyphenyl group, and a 4-((E)-2-phenylvinyl)phenyl group. The C-terminus is a primary amide.</p>	<p>C65H85N21O7</p>	<p>1272.523 <10%</p>
<p>Structure 1</p>  <p>Chemical structure of a protein derivative with a 1,2,3,4-tetrahydronaphthalene-1-carboxylic acid modification. The structure shows a protein backbone with various side chains, including a 2-phenyl-1H-imidazole-5-ylmethyl group, a 4-hydroxyphenyl group, and a 1,2,3,4-tetrahydronaphthalene-1-carboxylic acid group. The C-terminus is a primary amide.</p>	<p>C61H81N21O8</p>	<p>1236.4468 <10%</p>
<p>Structure 1</p>  <p>Chemical structure of a protein derivative with a 1,2,3,4-tetrahydronaphthalene-1-carboxylic acid modification. The structure shows a protein backbone with various side chains, including a 2-phenyl-1H-imidazole-5-ylmethyl group, a 4-hydroxyphenyl group, and a 1,2,3,4-tetrahydronaphthalene-1-carboxylic acid group. The C-terminus is a primary amide.</p>	<p>C67H85N21O7</p>	<p>1296.545 <10%</p>

 <p>Structure 1</p>	C65H83N21O7	1270.5072 <10%	
 <p>Structure 1</p>	C65H83N21O7	1270.5072 <10%	
 <p>Structure 1</p>	C58H81N21O8	1200.4138 <10%	

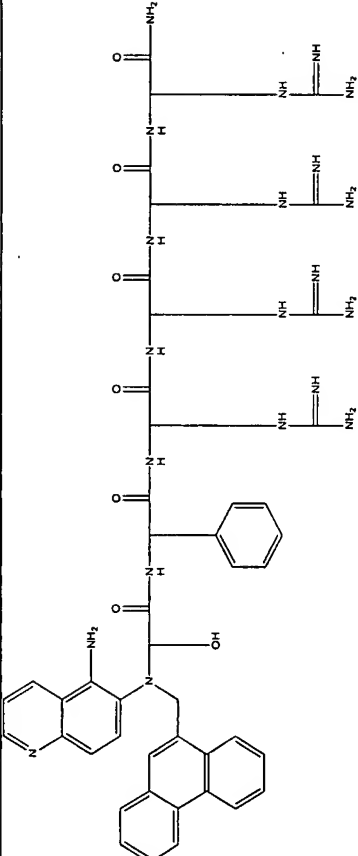
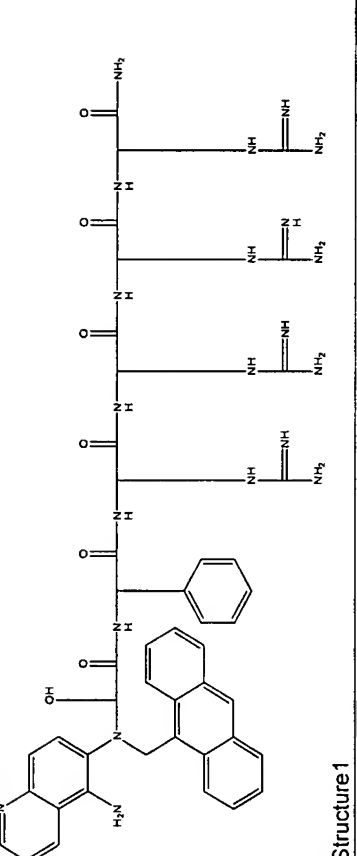
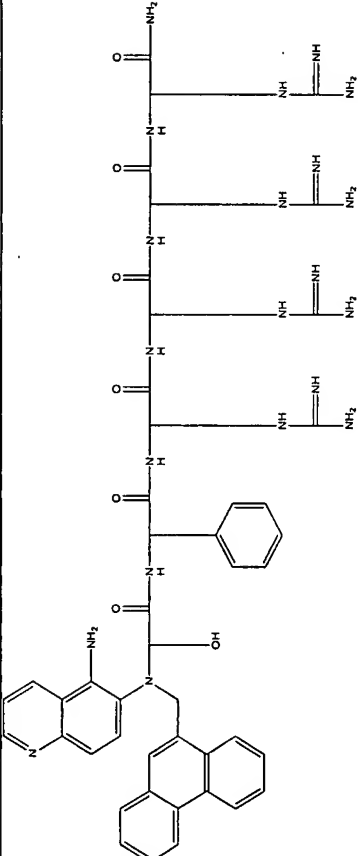
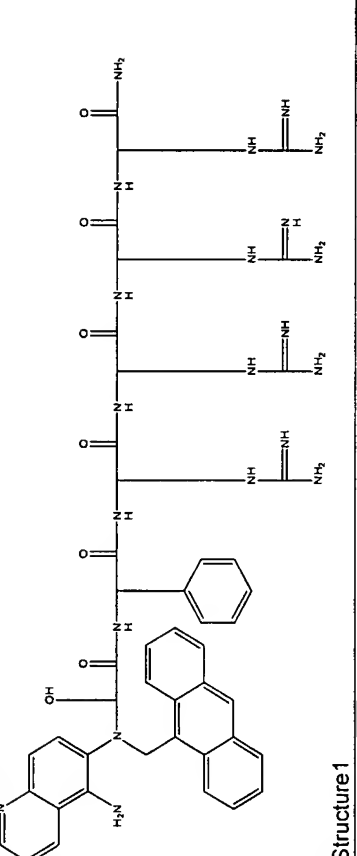
 <p>Structure 1</p>	C52H77N21O8	1124.3162	<10%
 <p>Structure 1</p>	C54H81N21O9	1168.3692	<10%
 <p>Structure 1</p>	C54H82N22O8	1167.3844	<10%

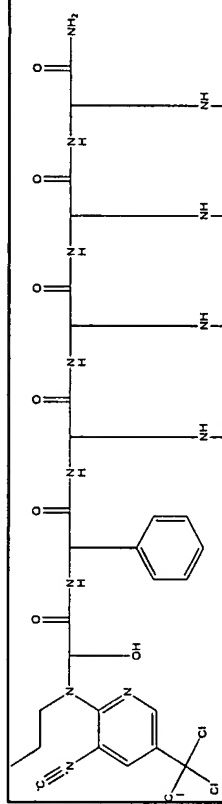
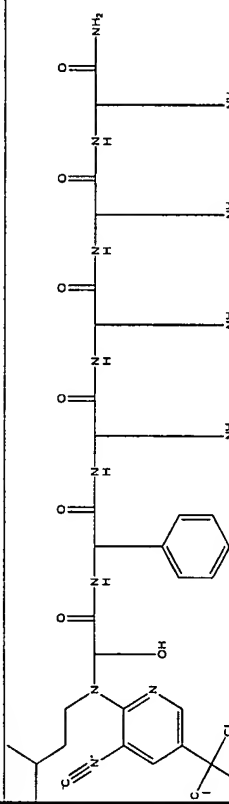
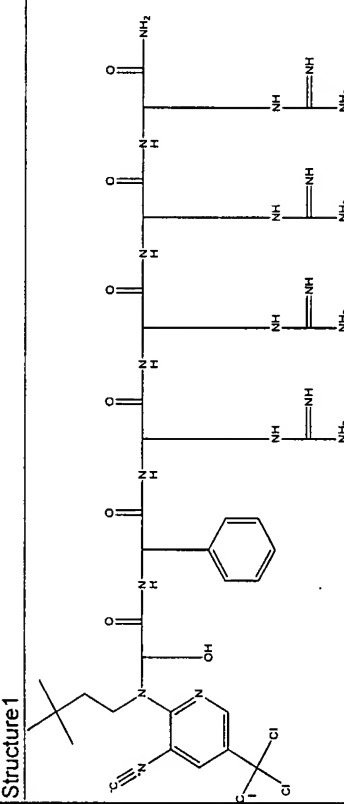
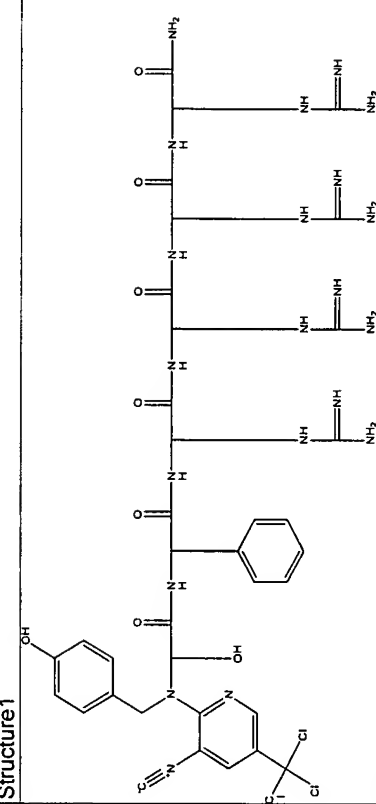
 <p>Structure 1</p>	C54H82N22O7	1151.385	<10%
 <p>Structure 1</p>	C52H78N22O9	1155.3302	<10%
 <p>Structure 1</p>	C52H76N22O9	1153.3144	<10%

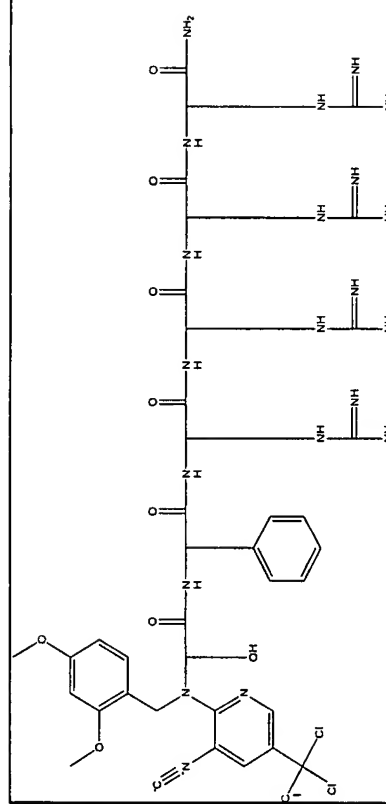
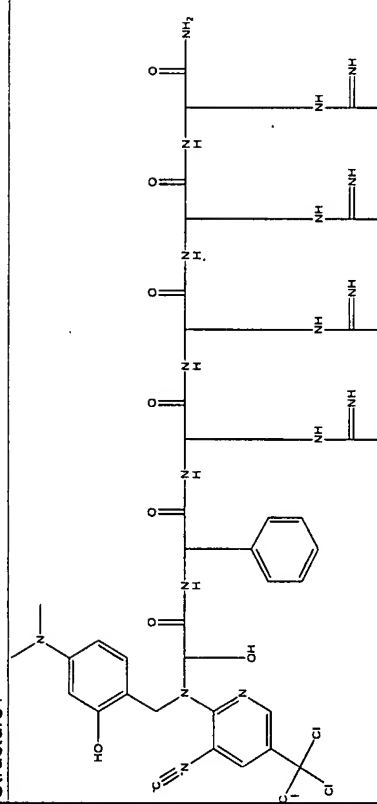
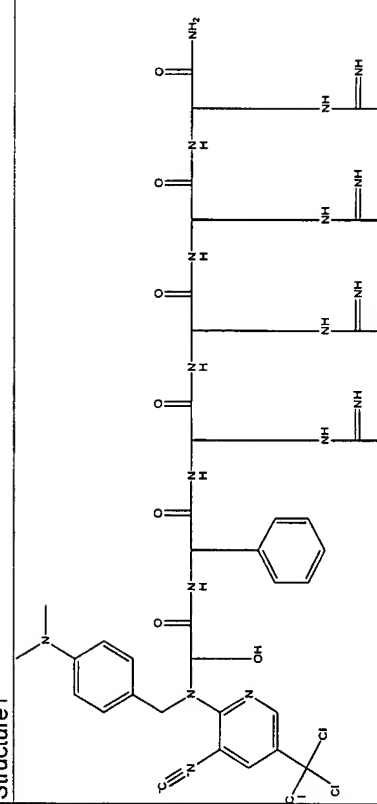
 <p>Chemical structure of a complex molecule featuring a quinoline ring system, a hydroxyl group, a nitro group, and a long chain of amide linkages with terminal amine groups.</p>	C52H76N22O10	1169.3138 <10%	
 <p>Chemical structure of a complex molecule featuring a quinoline ring system, a hydroxyl group, a chlorine atom, and a long chain of amide linkages with terminal amine groups.</p>	C52H75Cl2N21O7	1177.207 <10%	
 <p>Chemical structure of a complex molecule featuring a quinoline ring system, a hydroxyl group, a nitro group, and a long chain of amide linkages with terminal amine groups.</p>	C52H77N23O11	1200.3278 <10%	

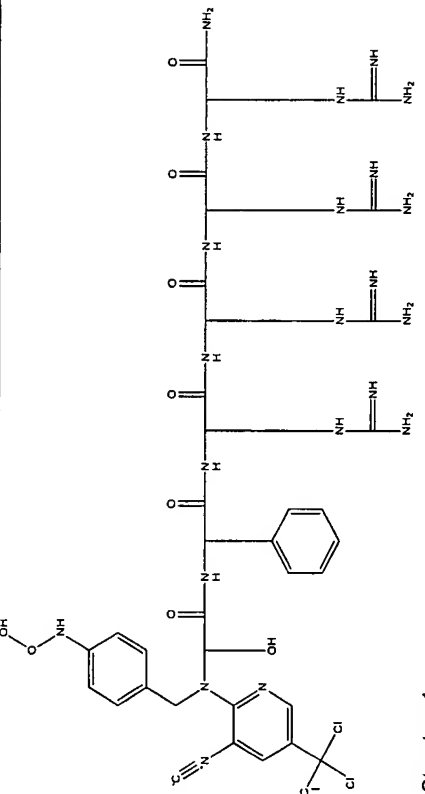
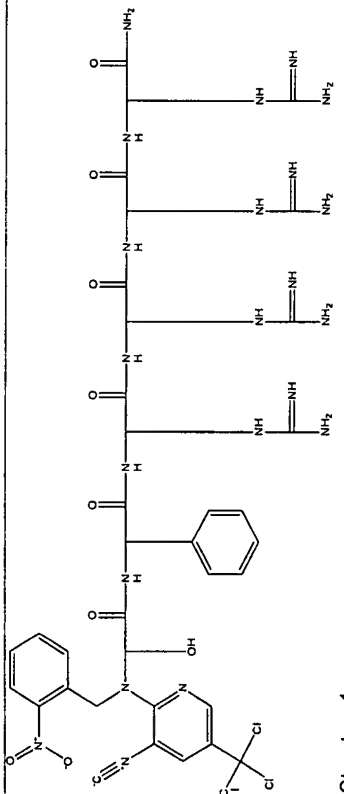
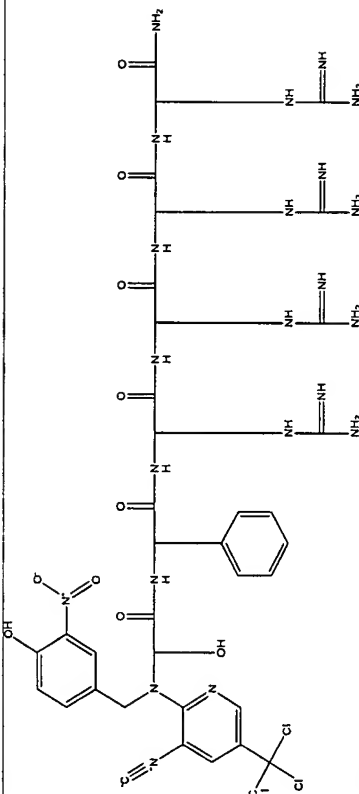
 <p>Structure 1</p>	C52H77N23O12	1216.3272 <10%	44
 <p>Structure 1</p>	C54H79N21O7	1134.3546 <10%	
 <p>Structure 1</p>	C56H84N22O7	1177.4228 <10%	
 <p>Structure 1</p>	C54H80N22O9	1181.368 <10%	

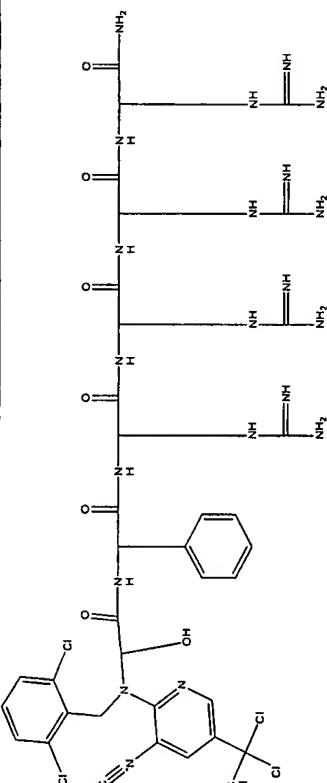
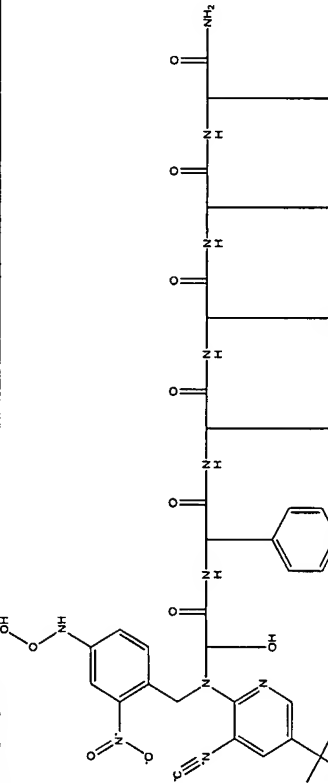
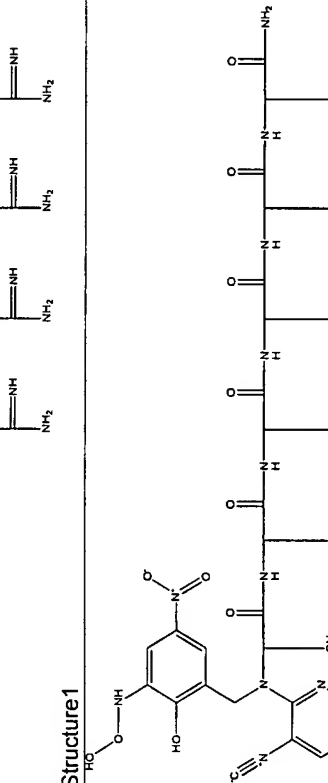
	C60H83N21O7	1210.4522	<10%
	C56H79N21O8	1174.376	<10%
	C62H83N21O7	1234.4742	<10%

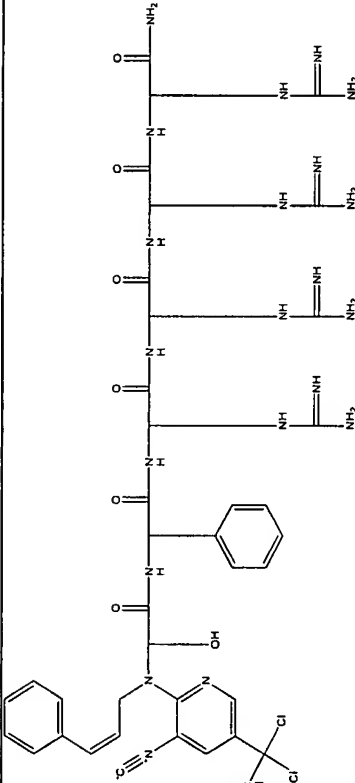
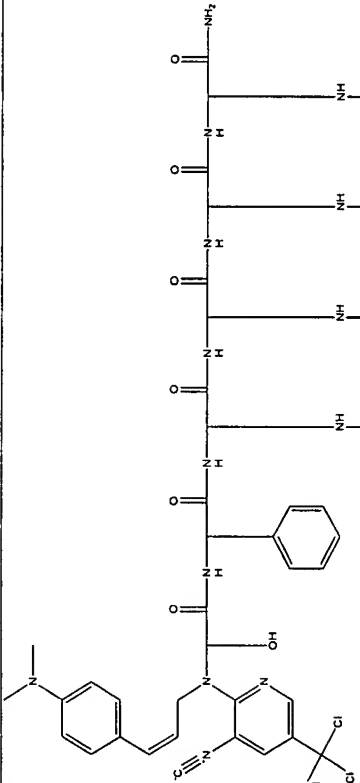
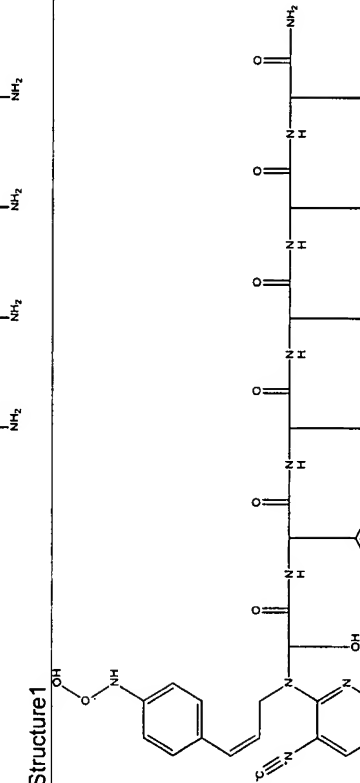
 <p>Structure 1</p>	C60H81N21O7	1208.4364 <10%	46
 <p>Structure 1</p>	C60H81N21O7	1208.4364 <10%	
 <p>Structure 1</p>	C53H79N21O8	1138.343 <10%	
 <p>Structure 1</p>	C53H79N21O8	1154.3424 <10%	

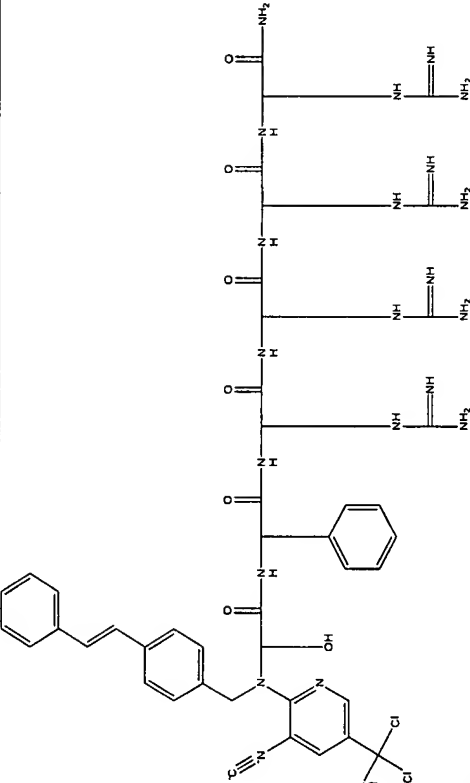
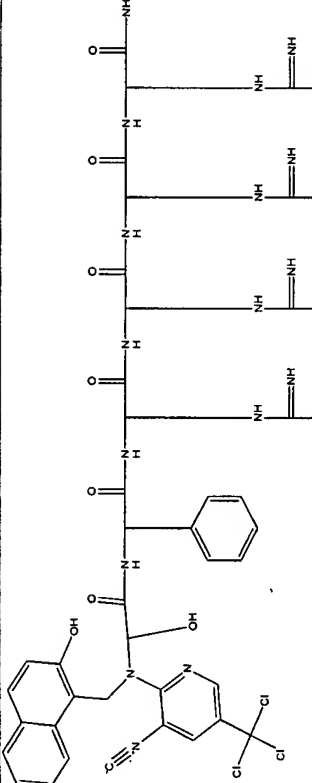
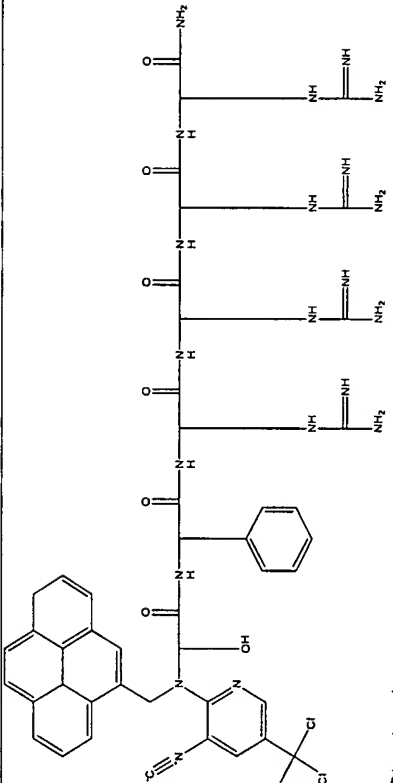
 <p>Structure 1</p>	C46H72Cl3N21O7	1137.5703	<10%
 <p>Structure 1</p>	C48H76Cl3N21O7	1165.6239	<10%
 <p>Structure 1</p>	C49H78Cl3N21O7	1179.6507	<10%
 <p>Structure 1</p>	C50H72Cl3N21O8	1201.6137	<10%

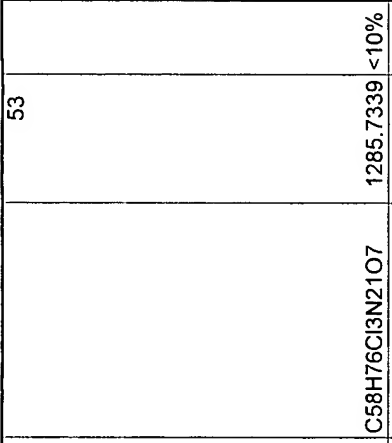
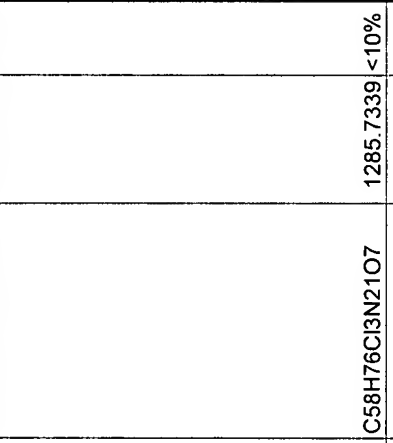
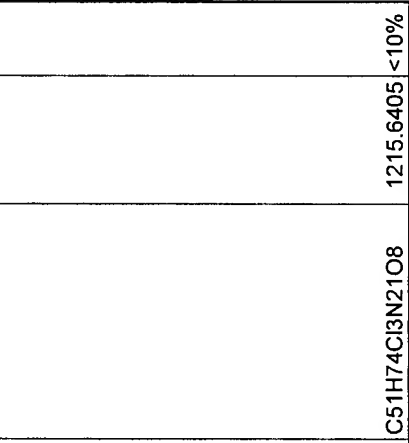
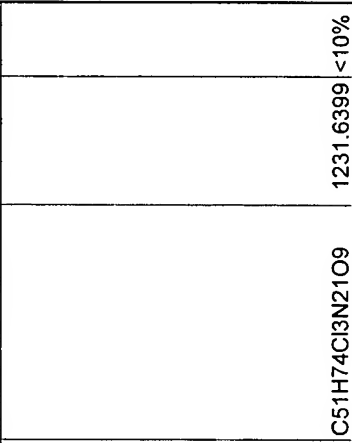
 <p>Structure 1</p>	C52H76Cl3N21O9	1245.6667	<10%
 <p>Structure 1</p>	C52H77Cl3N22O8	1244.6819	<10%
 <p>Structure 1</p>	C52H77Cl3N22O7	1228.6825	<10%

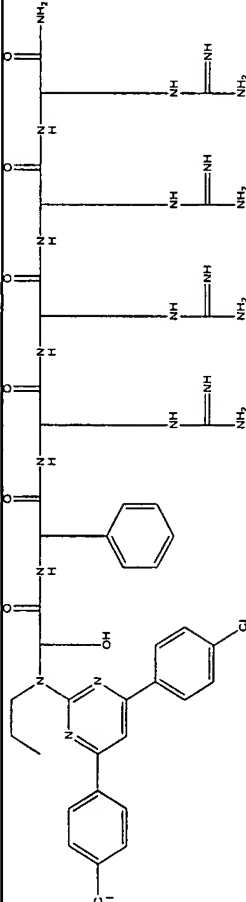
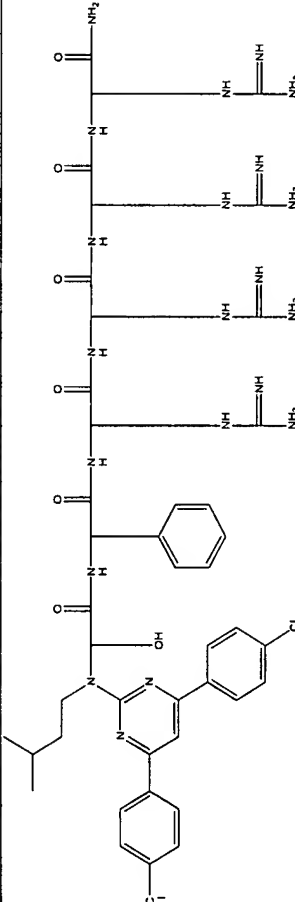
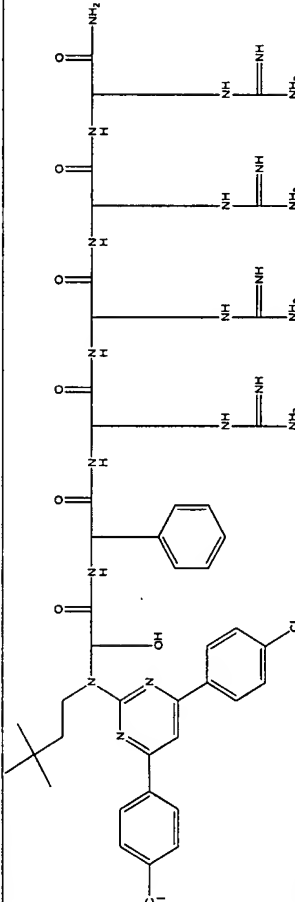
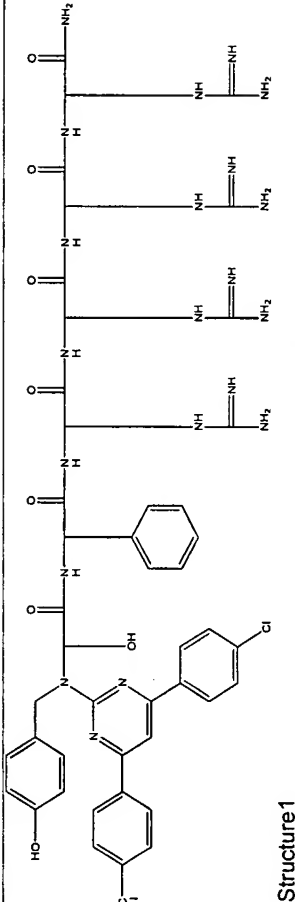
 <p>Structure 1</p>	C50H73Cl3N22O9	1232.6277	<10%
 <p>Structure 1</p>	C50H71Cl3N22O10	1230.6119	<10%
 <p>Structure 1</p>	C50H71Cl3N22O10	1246.6113	<10%

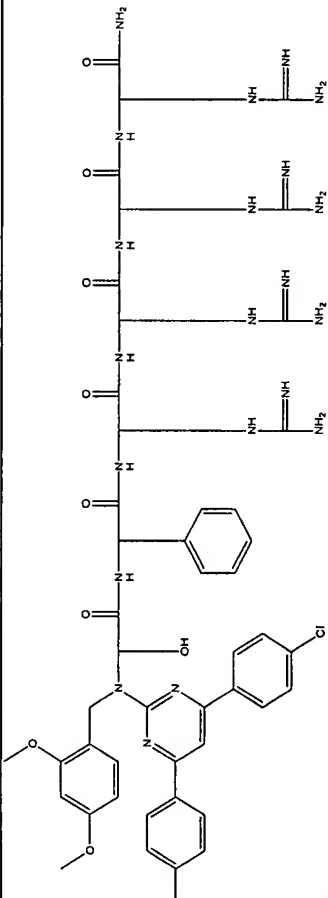
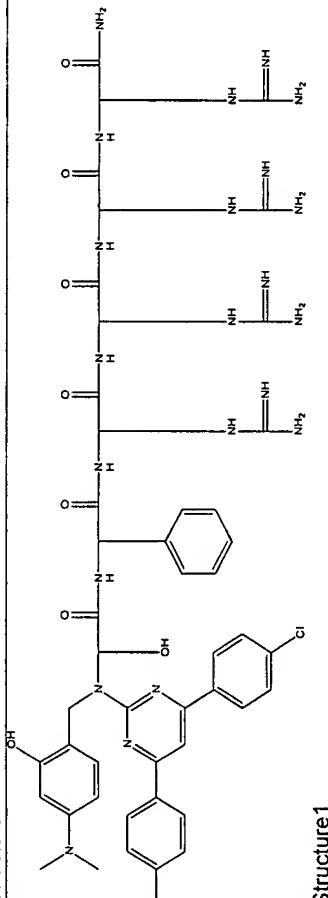
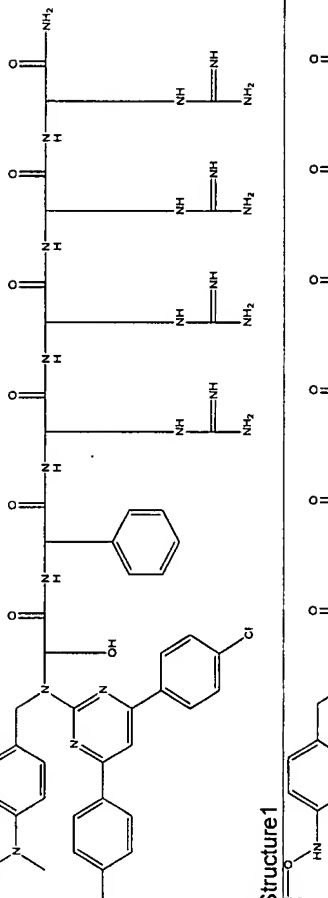
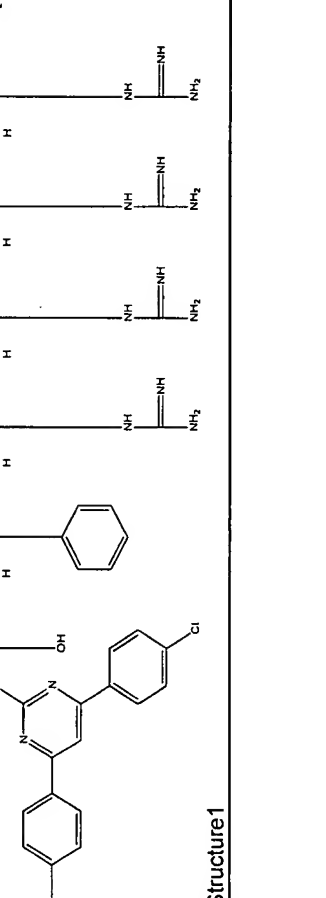
 <p>Structure 1</p>	C50H70Cl5N21O7	1254.5045 <10%	
 <p>Structure 1</p>	C50H72Cl3N23O11	1277.6253 <10%	
 <p>Structure 1</p>	C50H72Cl3N23O12	1293.6247 <10%	

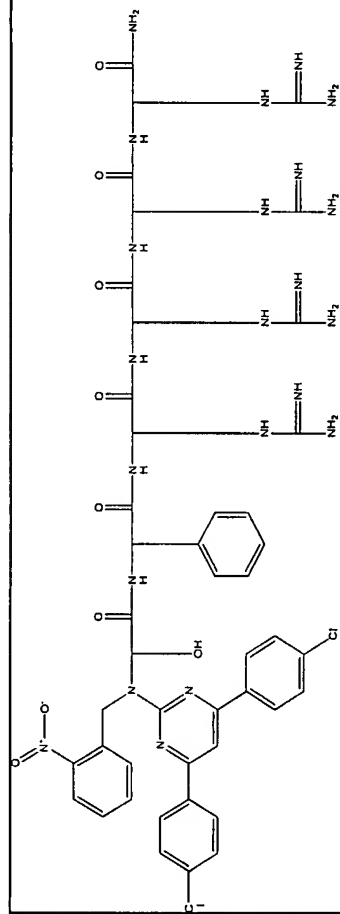
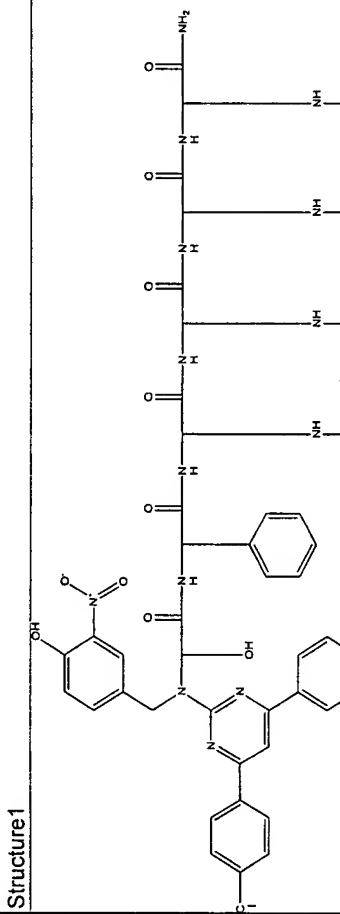
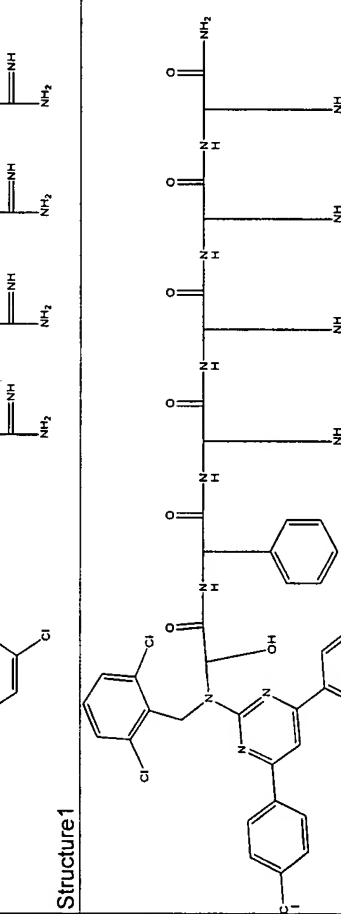
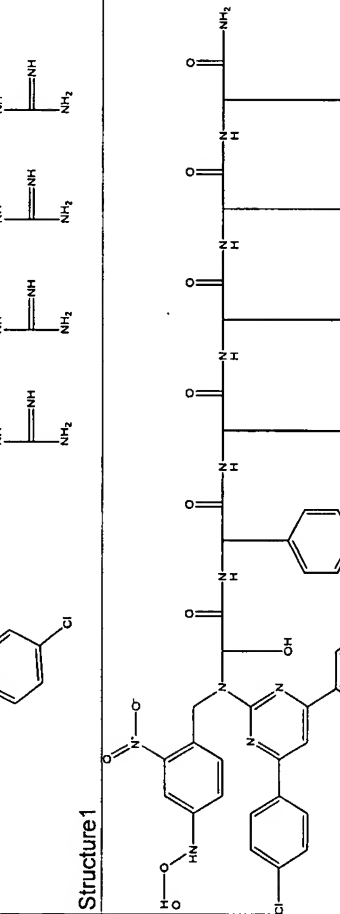
 <p>Structure 1</p>	C52H74Cl3N21O7	1211.6521 <10%	
 <p>Structure 1</p>	C54H79Cl3N22O7	1254.7203 <10%	
 <p>Structure 1</p>	C52H75Cl3N22O9	1258.6655 <10%	

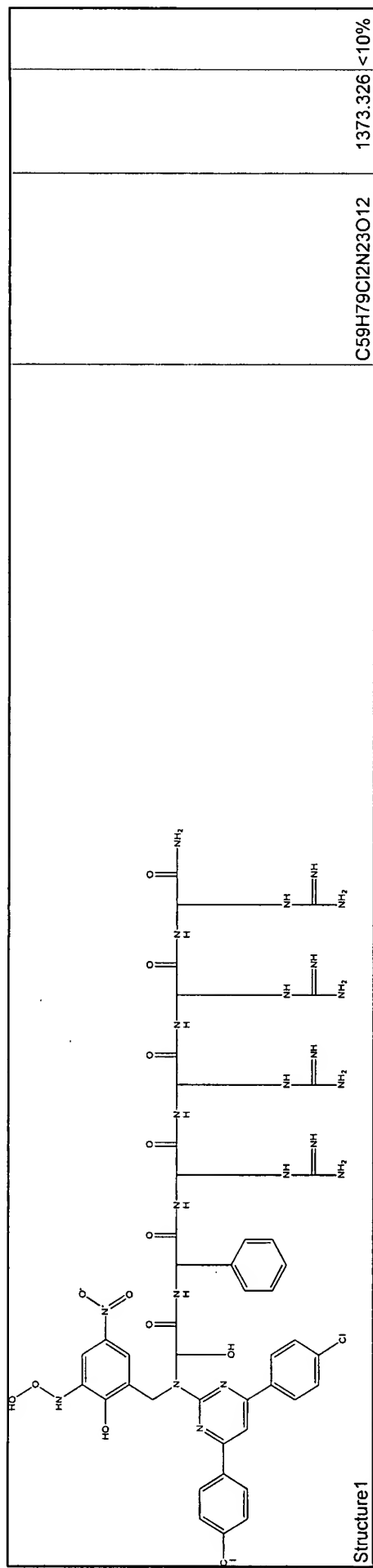
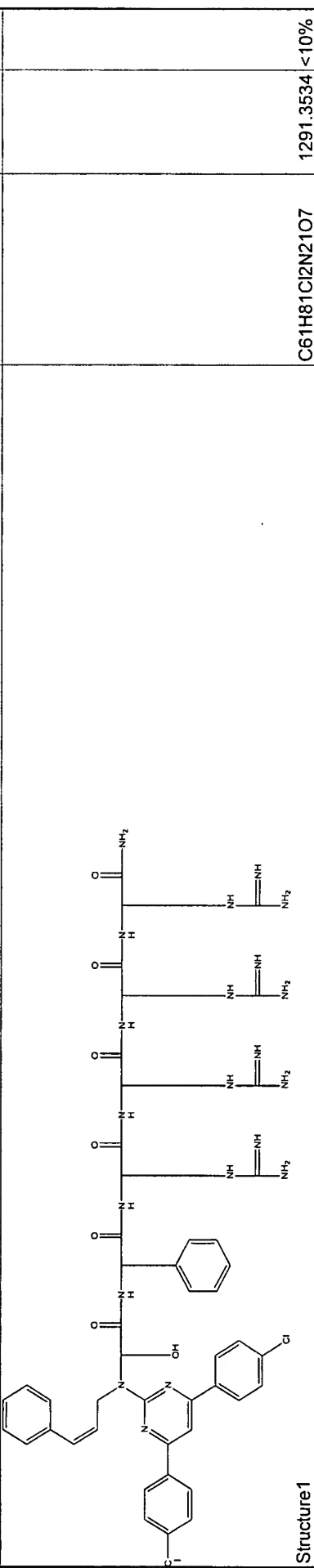
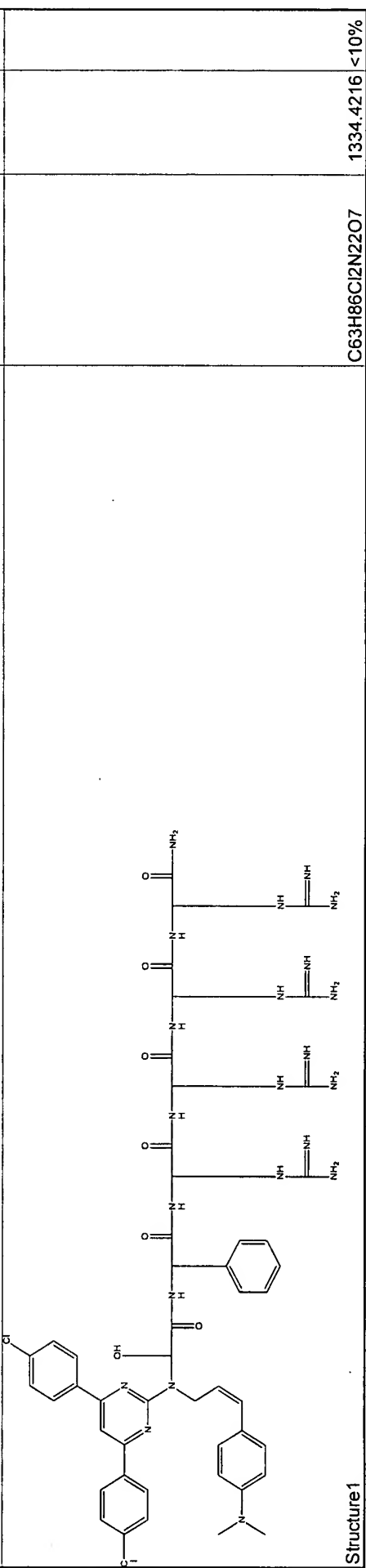
 <p>Structure 1</p>	C58H78Cl3N21O7	1287.7497 <10%	
 <p>Structure 1</p>	C54H74Cl3N21O8	1251.6735 <10%	
 <p>Structure 1</p>	C60H78Cl3N21O7	1311.7717 <10%	

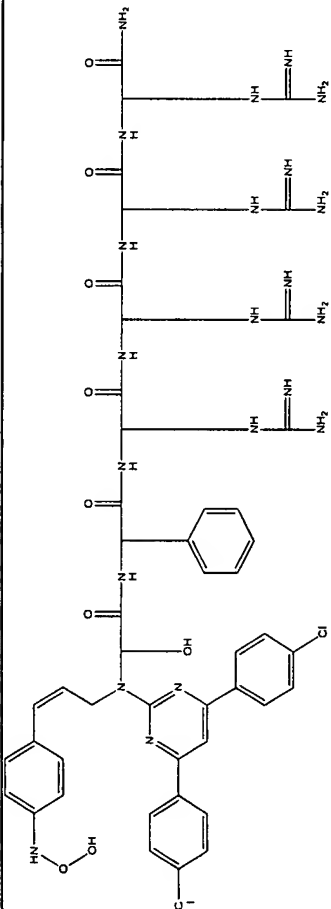
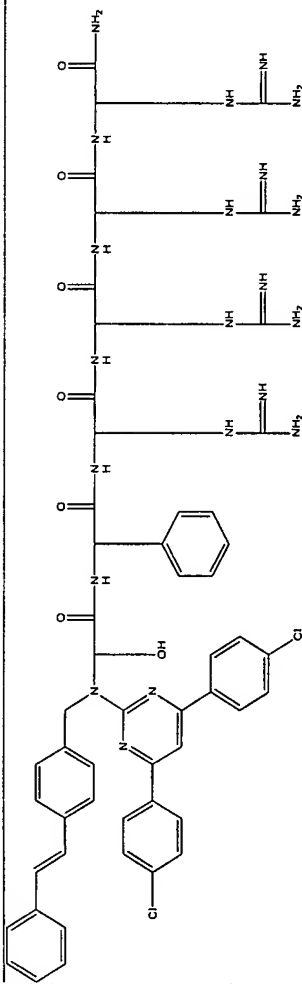
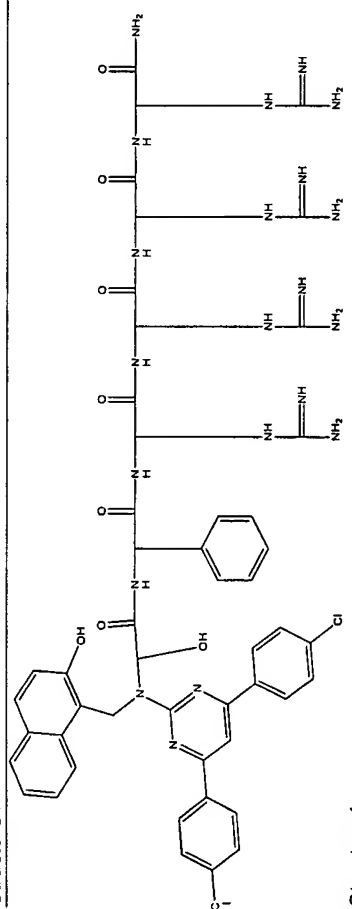
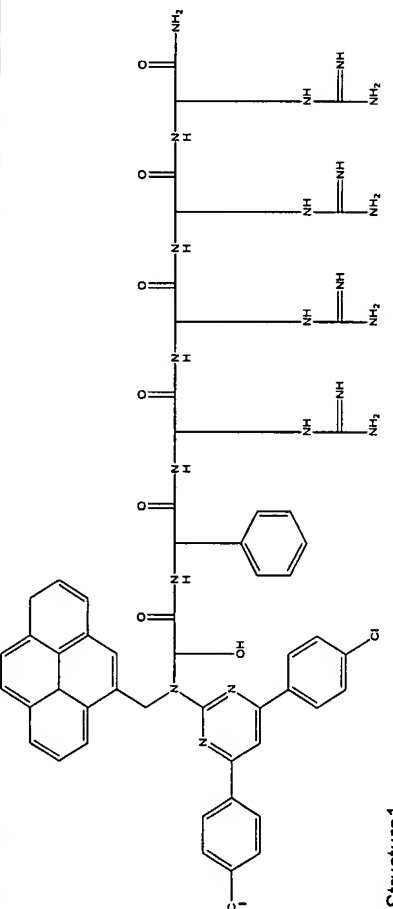
 <p>Structure 1</p>	<p>C58H76Cl3N21O7</p>	<p>1285.7339 <10%</p>	<p>53</p>
 <p>Structure 1</p>	<p>C58H76Cl3N21O7</p>	<p>1285.7339 <10%</p>	
 <p>Structure 1</p>	<p>C51H74Cl3N21O8</p>	<p>1215.6405 <10%</p>	
 <p>Structure 1</p>	<p>C51H74Cl3N21O9</p>	<p>1231.6399 <10%</p>	

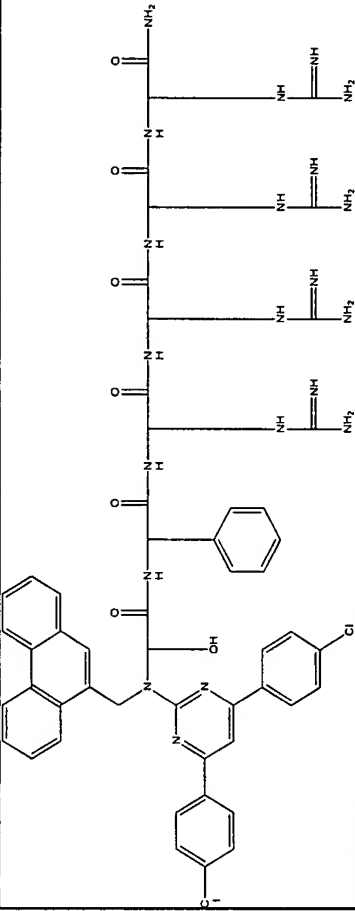
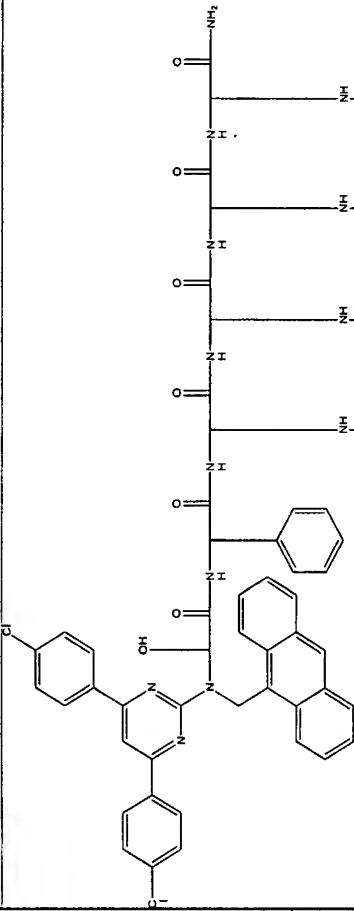
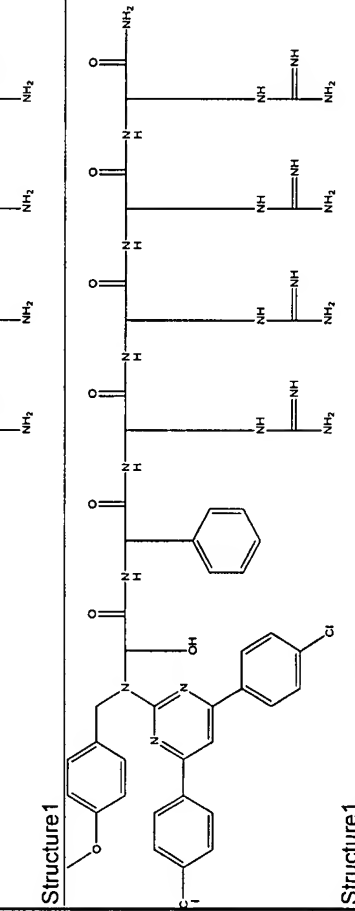
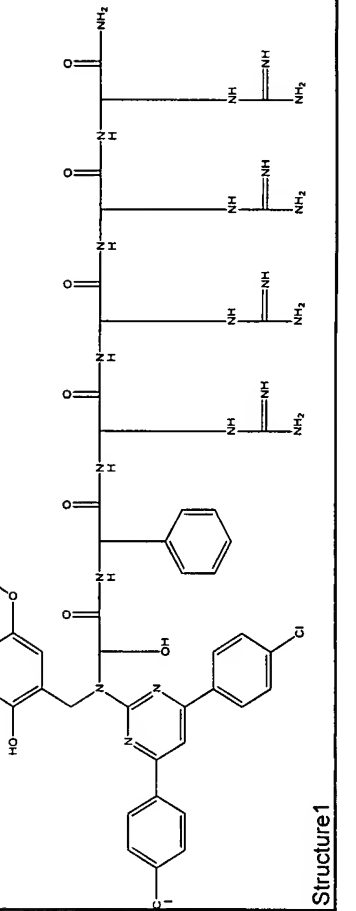
 <p>Structure 1</p>	C55H79Cl2N21O7	1217.2716 <10%	
 <p>Structure 1</p>	C57H83Cl2N21O7	1245.3252 <10%	
 <p>Structure 1</p>	C58H85Cl2N21O7	1259.352 <10%	
 <p>Structure 1</p>	C59H79Cl2N21O8	1281.315 <10%	

 <p>Structure 1</p>	C61H83Cl2N21O9	1325.368	<10%
 <p>Structure 1</p>	C61H84Cl2N22O8	1324.3832	<10%
 <p>Structure 1</p>	C61H84Cl2N22O7	1308.3838	<10%
 <p>Structure 1</p>	C59H80Cl2N22O9	1312.329	<10%

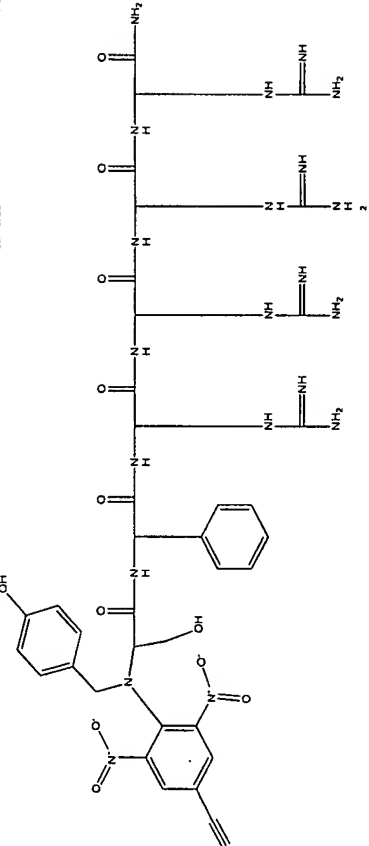
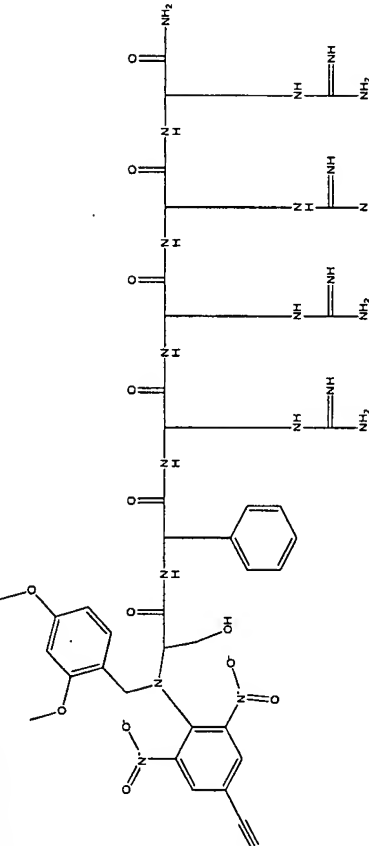
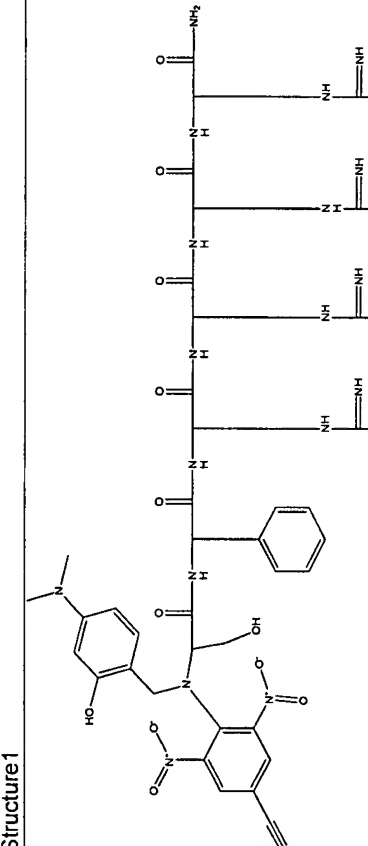
 <p>Structure 1</p>	C59H78Cl2N22O9	1310.3132	<10%
 <p>Structure 1</p>	C59H78Cl2N22O10	1326.3126	<10%
 <p>Structure 1</p>	C59H77Cl4N21O7	1334.2058	<10%
 <p>Structure 1</p>	C59H79Cl2N23O11	1357.3266	<10%

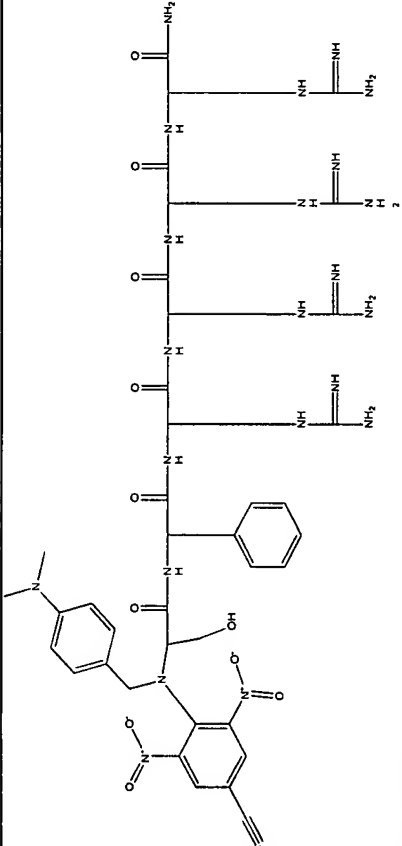
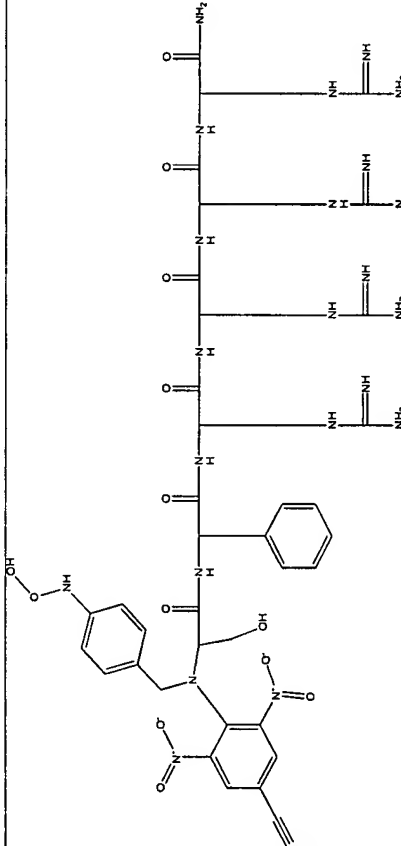
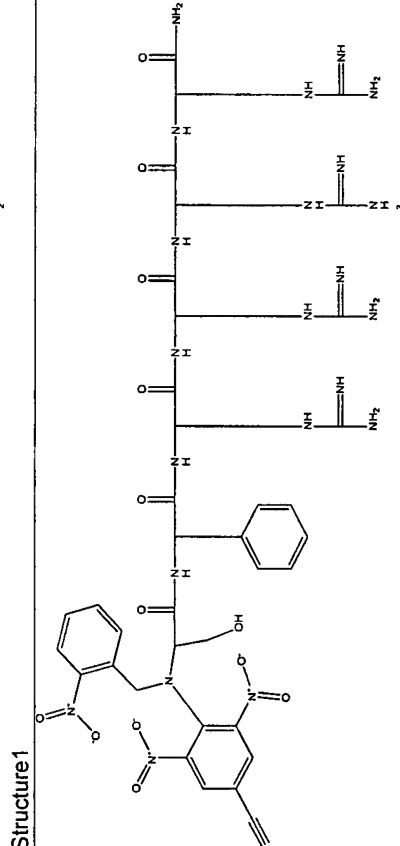
 <p>Structure 1</p>	C59H79Cl2N23O12	1373.326	<10%
 <p>Structure 1</p>	C61H81Cl2N21O7	1291.3534	<10%
 <p>Structure 1</p>	C63H86Cl2N22O7	1334.4216	<10%

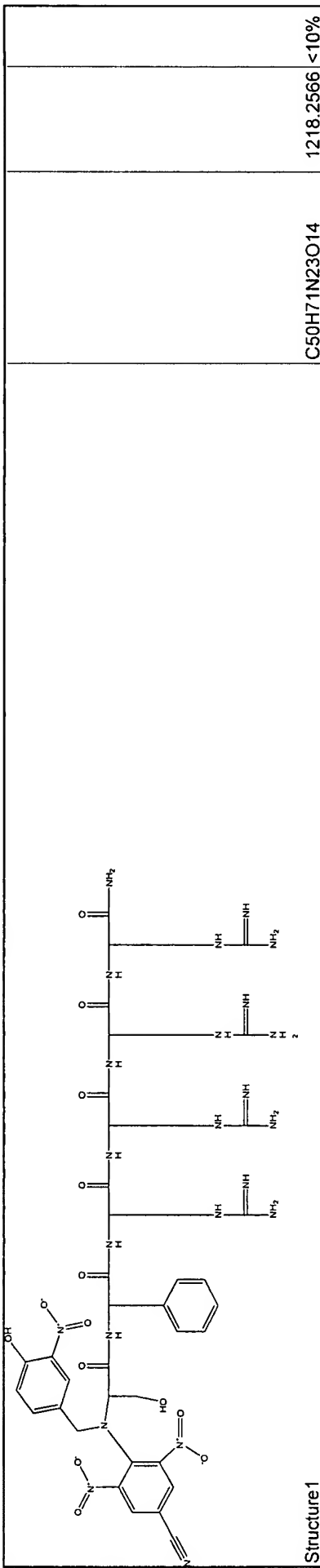
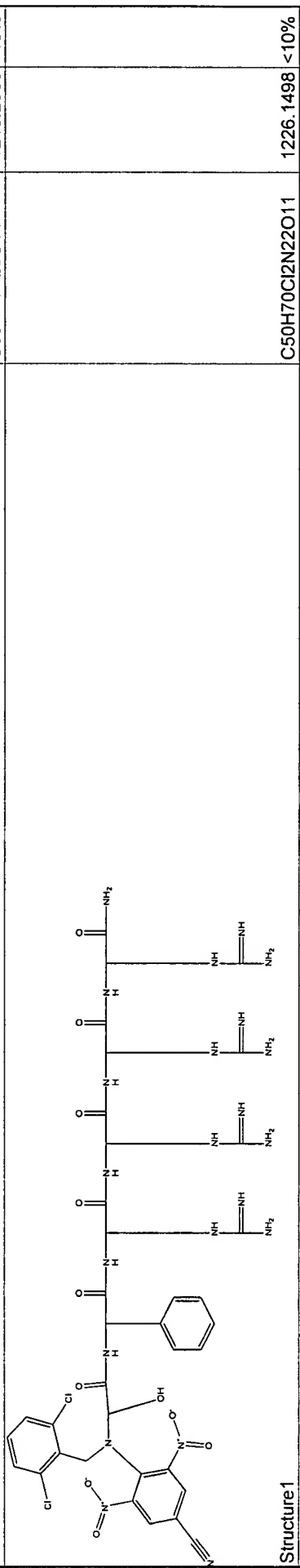
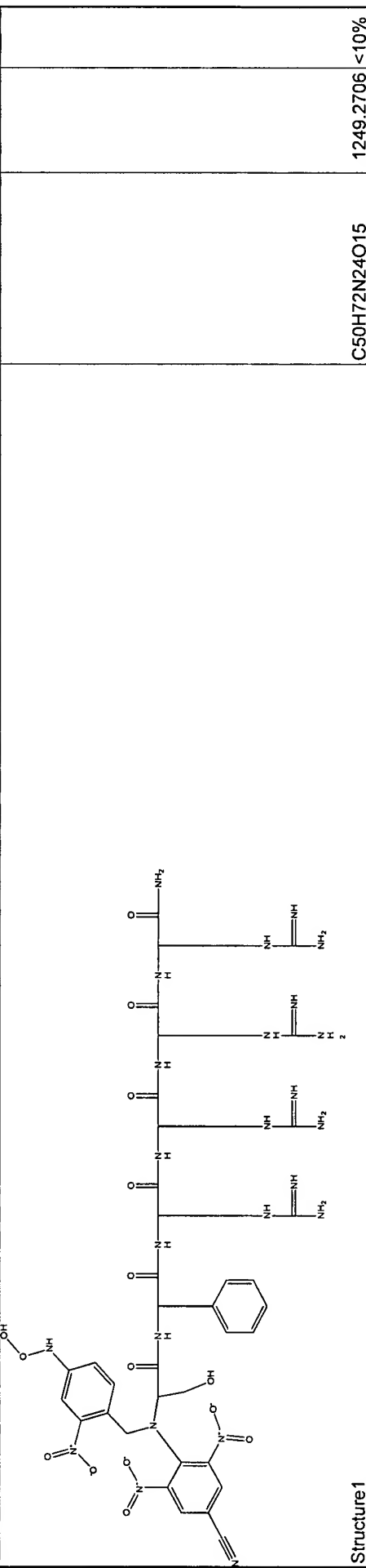
 <p>Structure 1</p>	C61H82Cl2N22O9	1338.3668	<10%
 <p>Structure 1</p>	C67H85Cl2N21O7	1367.451	<10%
 <p>Structure 1</p>	C63H81Cl2N21O8	1331.3748	<10%
 <p>Structure 1</p>	C69H85Cl2N21O7	1391.473	<10%

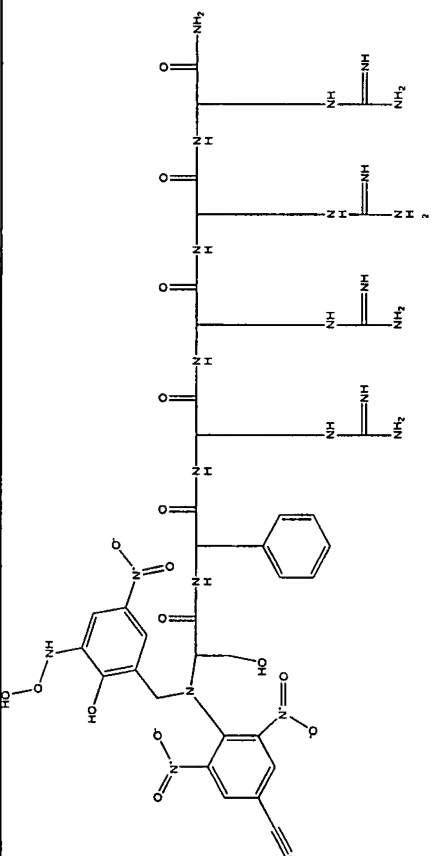
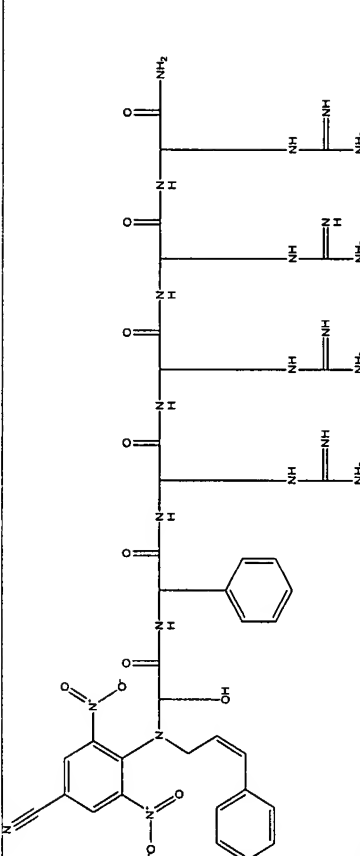
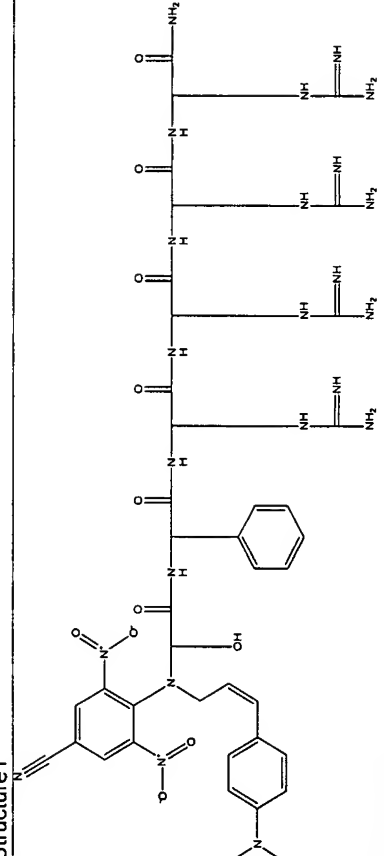
 <p>Structure 1</p>	C67H83Cl2N21O7	1365.4352 <10%	
 <p>Structure 1</p>	C67H83Cl2N21O7	1365.4352 <10%	
 <p>Structure 1</p>	C60H81Cl2N21O8	1295.3418 <10%	
 <p>Structure 1</p>	C60H81Cl2N21O9	1311.3412 <10%	

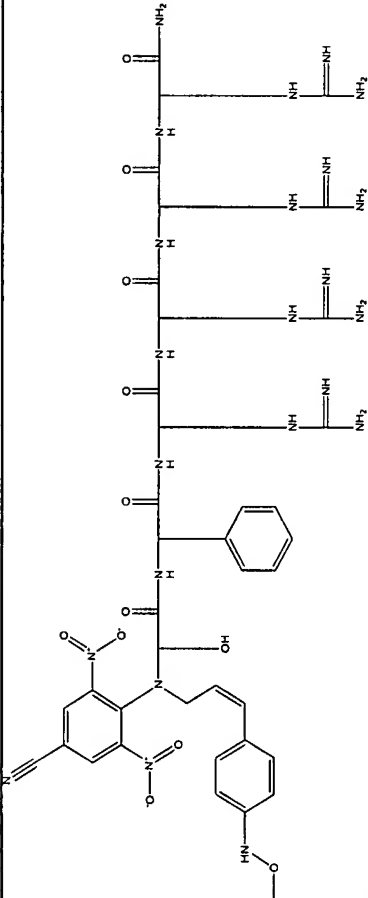
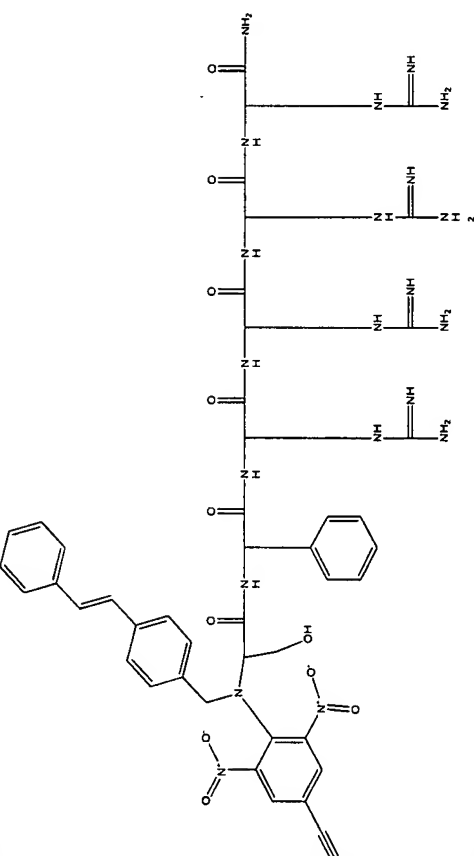
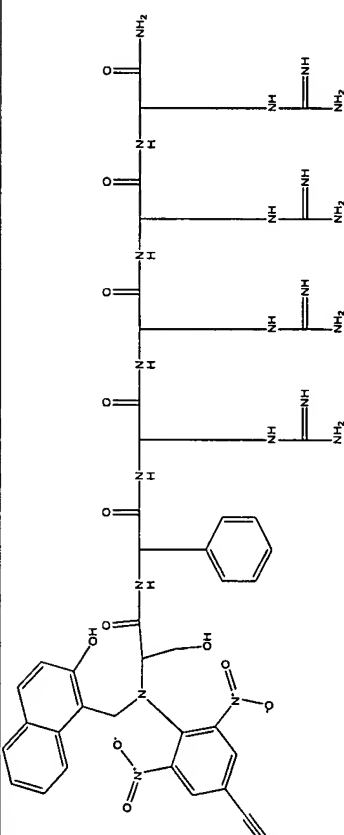
	C46H72N22O11	1109.2156 <10%	
	C48H76N22O11	1137.2692 <10%	
	C49H78N22O11	1151.296 <10%	

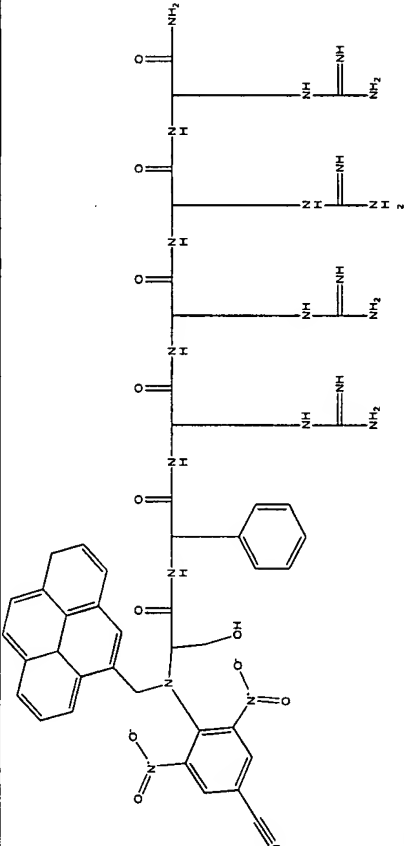
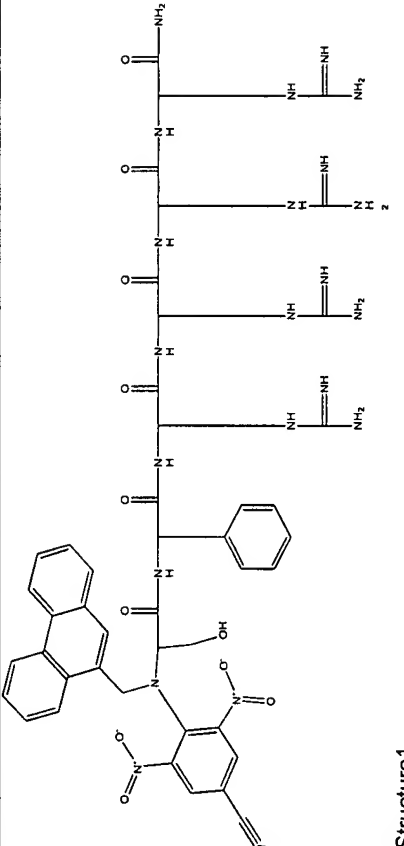
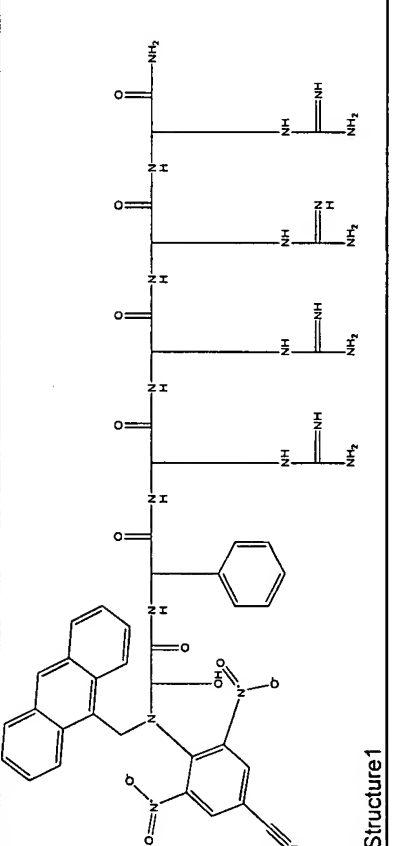
 <p>Structure 1</p>	C50H72N22O12	1173.259 <10%	
 <p>Structure 1</p>	C52H76N22O13	1217.312 <10%	
 <p>Structure 1</p>	C52H77N23O12	1216.3272 <10%	

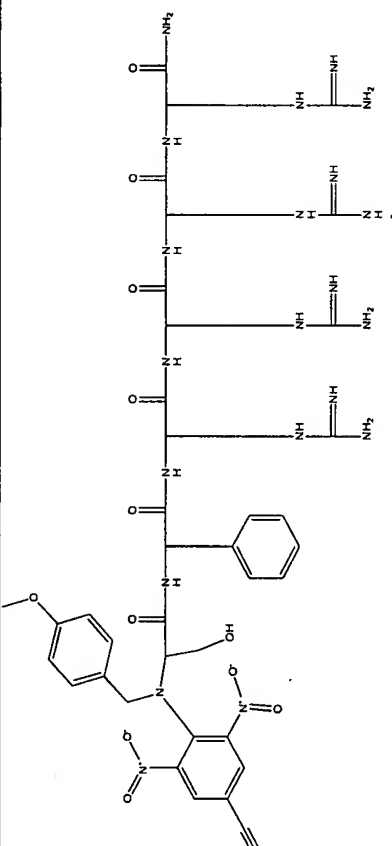
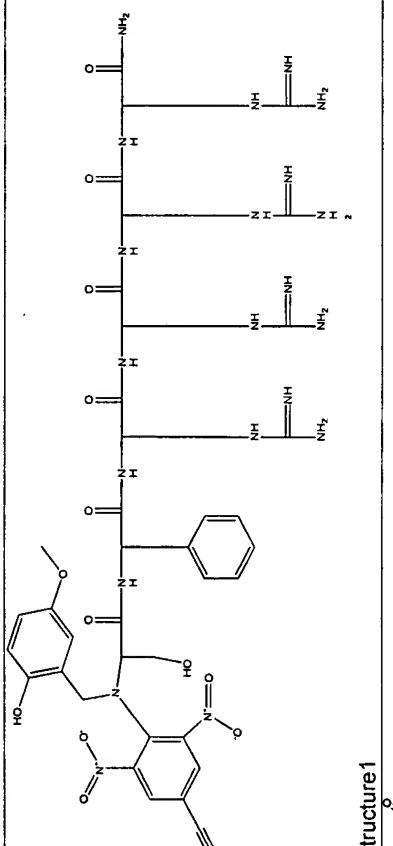
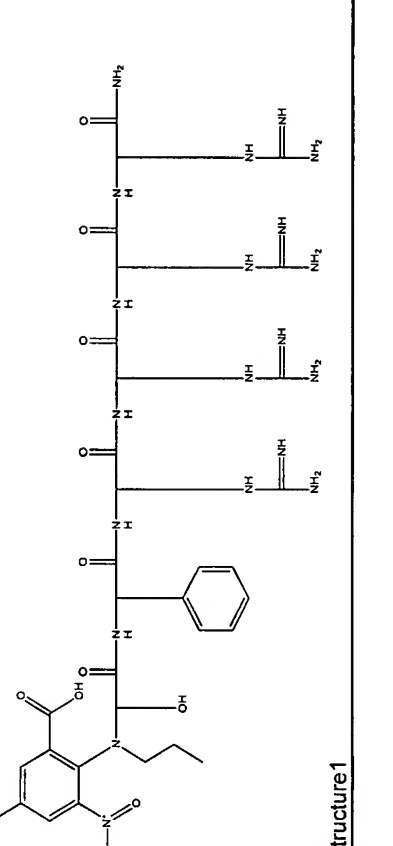
 <p>Structure 1</p>	C52H77N23O11	1200.3278 <10%	
 <p>Structure 1</p>	C50H73N23O13	1204.273 <10%	
 <p>Structure 1</p>	C50H71N23O13	1202.2572 <10%	

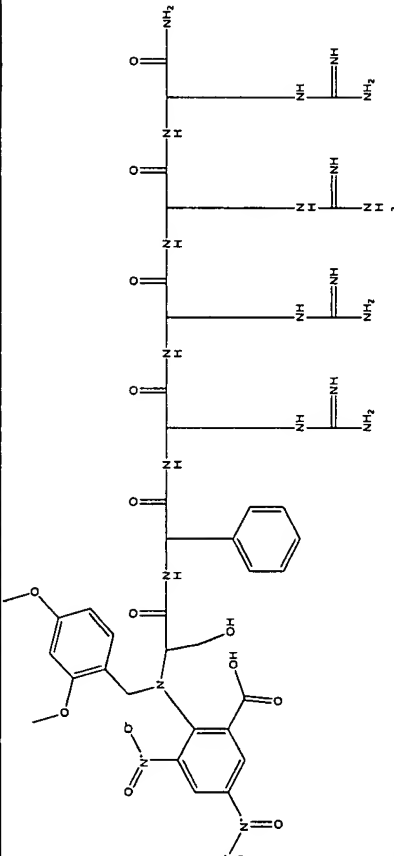
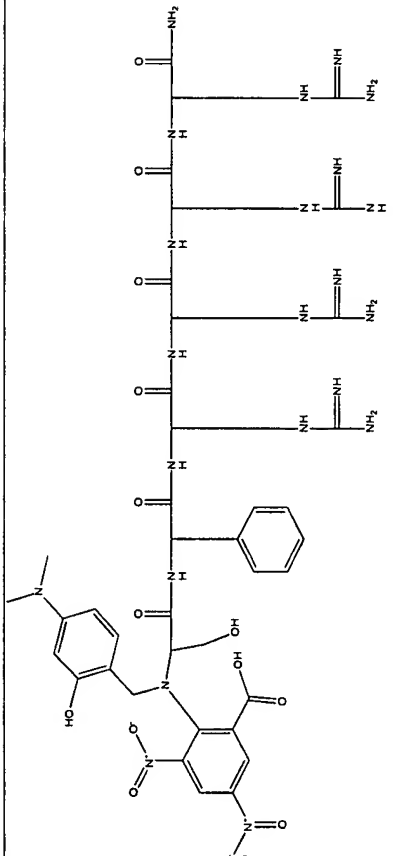
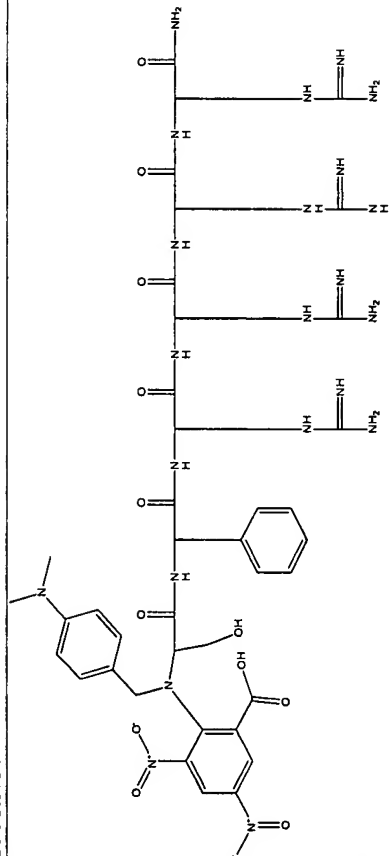
	C50H71N23O14	1218.2566	<10%
	C50H70Cl2N22O11	1226.1498	<10%
	C50H72N24O15	1249.2706	<10%

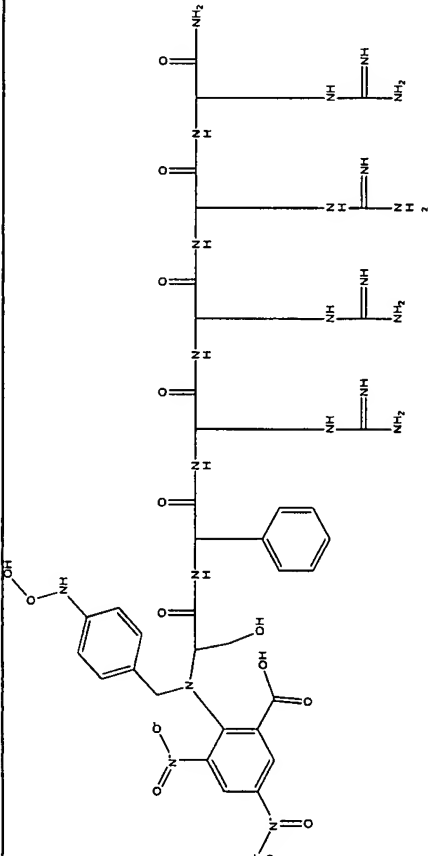
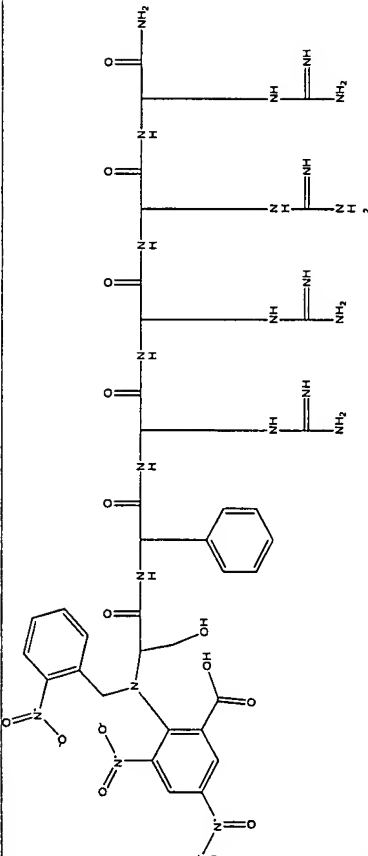
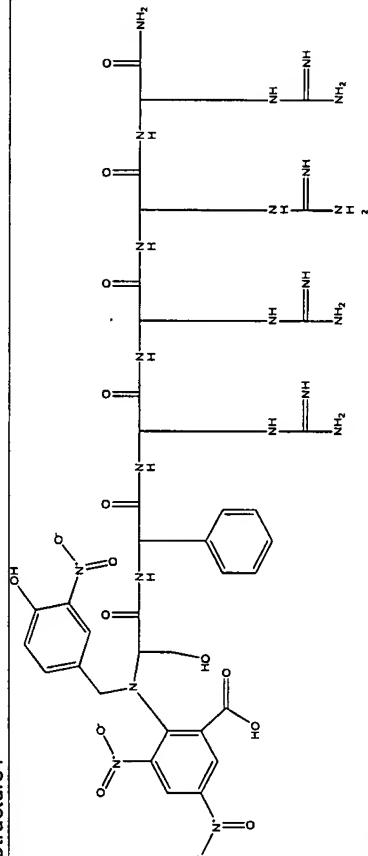
 <p>Structure 1</p>	C50H72N24O16	1265.27	<10%
 <p>Structure 1</p>	C52H74N22O11	1183.2974	<10%
 <p>Structure 1</p>	C54H79N23O11	1226.3656	<10%

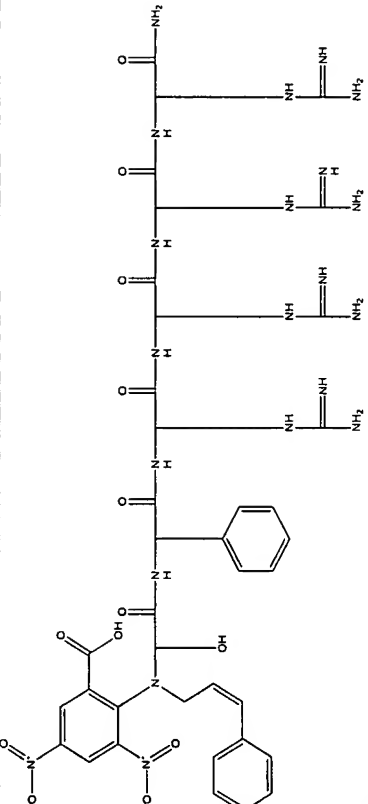
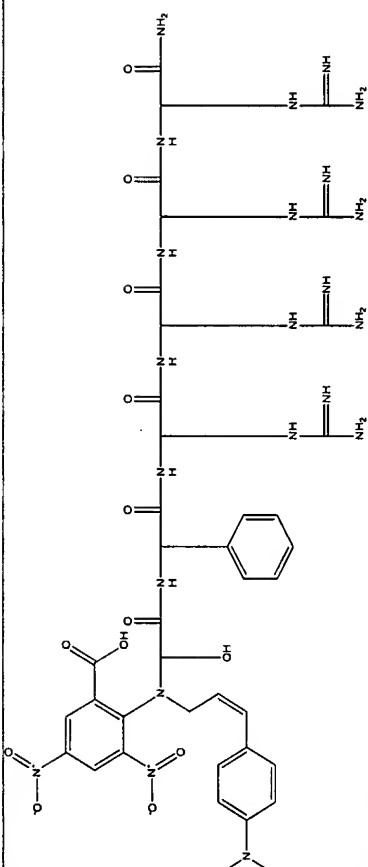
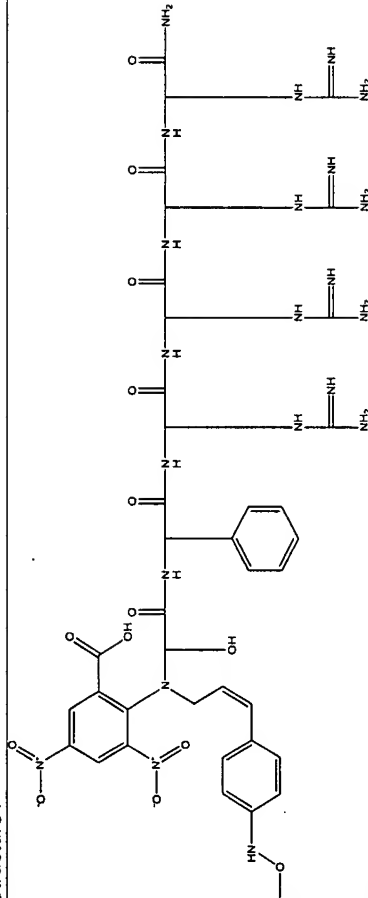
 <p>Structure 1</p>	C52H75N23O13	1230.3108 <10%	
 <p>Structure 1</p>	C58H78N22O11	1259.395 <10%	
 <p>Structure 1</p>	C54H74N22O12	1223.3188 <10%	

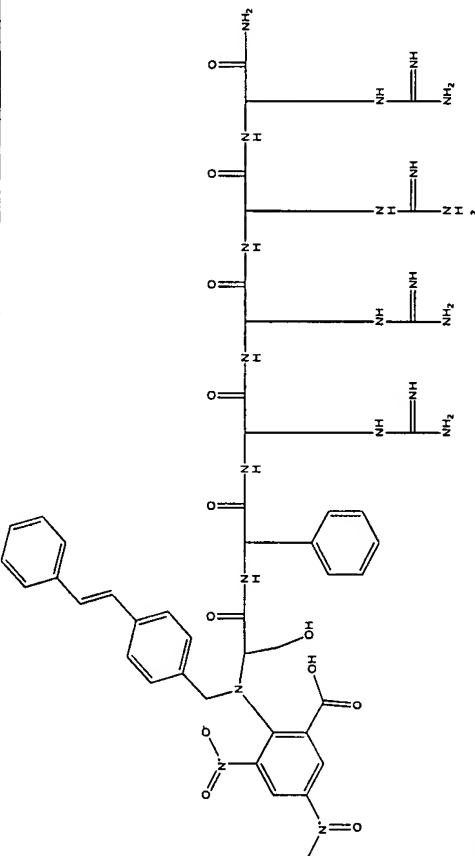
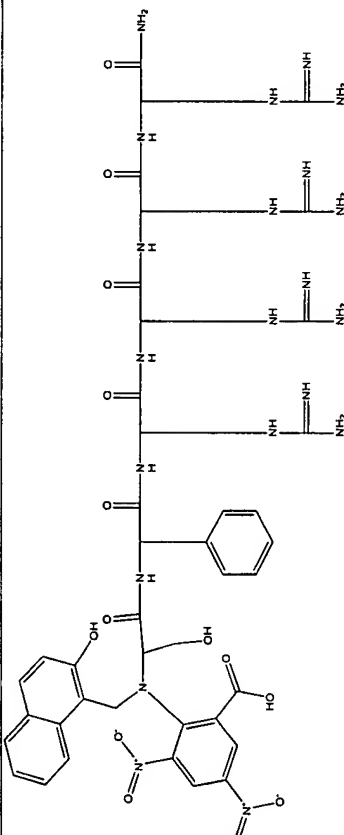
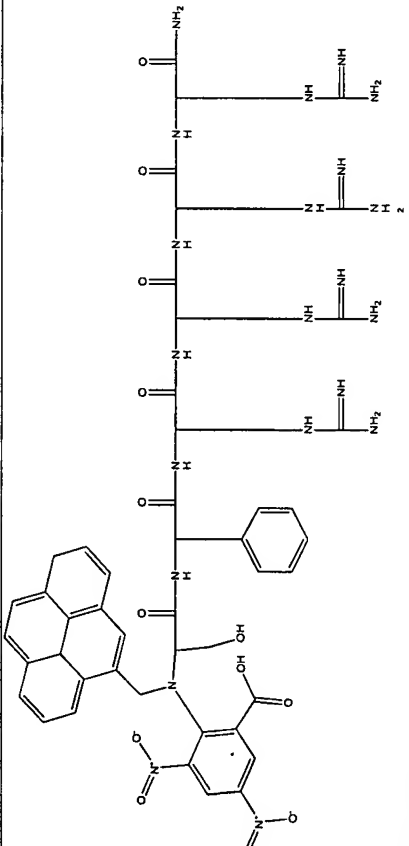
 <p>Structure 1</p>	C60H78N22O11	1283.417 <10%	
 <p>Structure 1</p>	C58H76N22O11	1257.3792 <10%	
 <p>Structure 1</p>	C58H76N22O11	1257.3792 <10%	

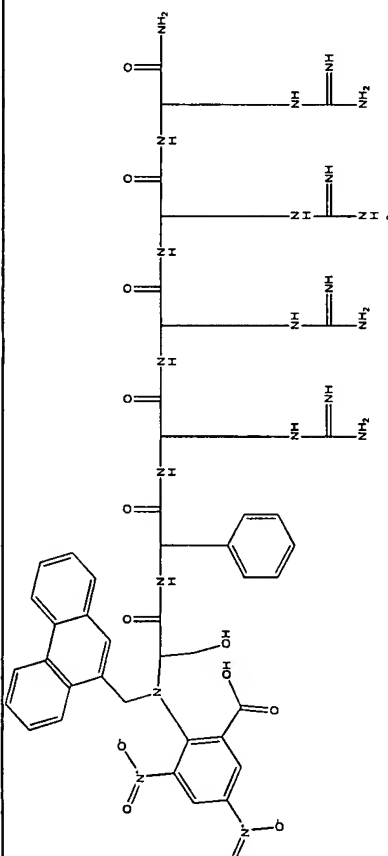
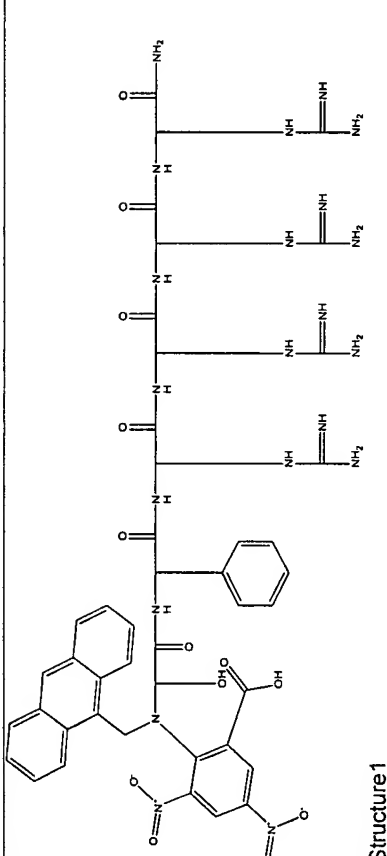
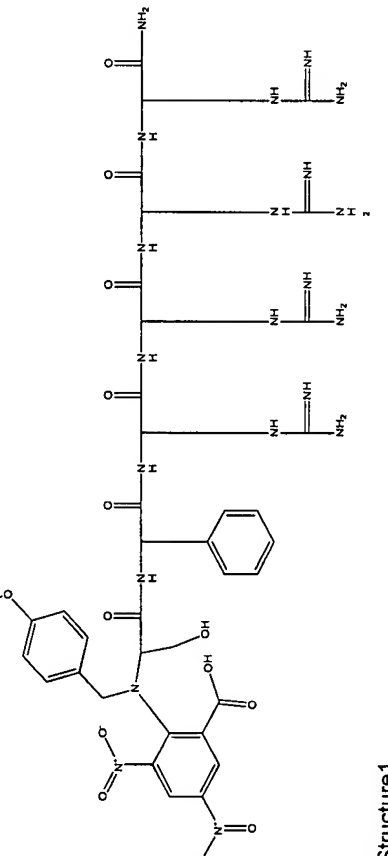
 <p>Structure 1</p>	C51H74N22O12	1187.2858	<10%
 <p>Structure 1</p>	C51H74N22O13	1203.2852	<10%
 <p>Structure 1</p>	C46H73N21O13	1128.2156	<10%

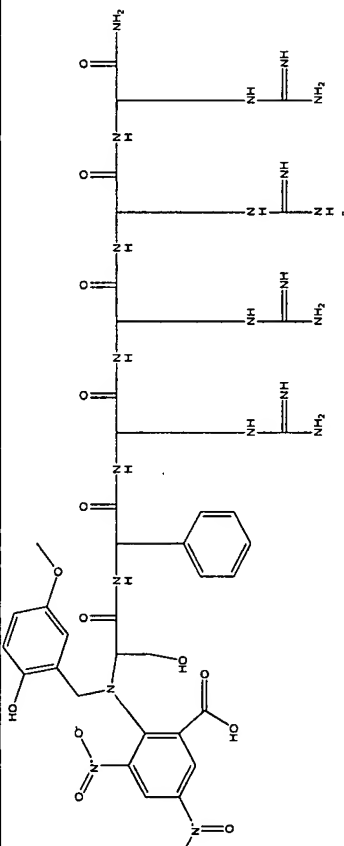
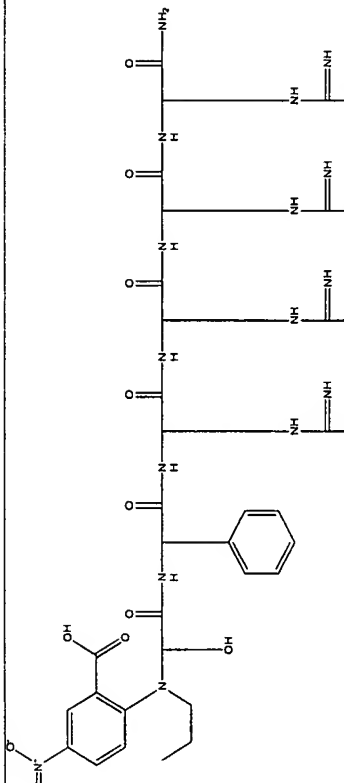
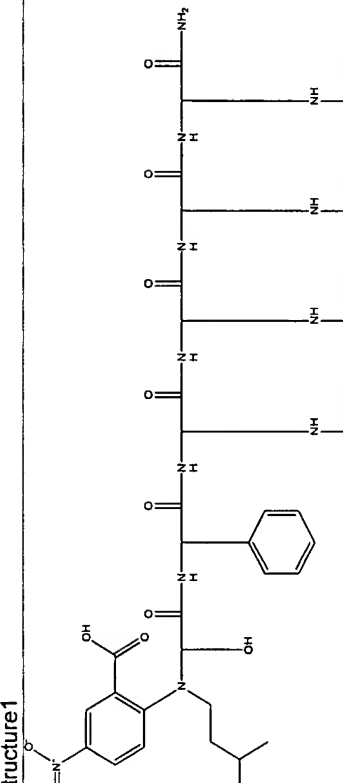
 <p>Structure 1</p>	C52H77N21O15	1236.312 <10%	
 <p>Structure 1</p>	C52H78N22O14	1235.3272 <10%	
 <p>Structure 1</p>	C52H78N22O13	1219.3278 <10%	

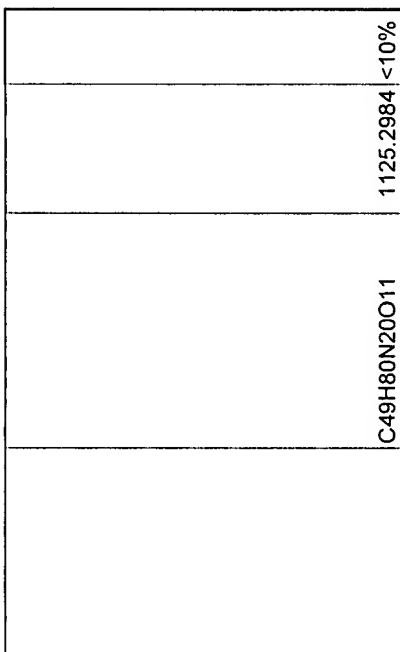
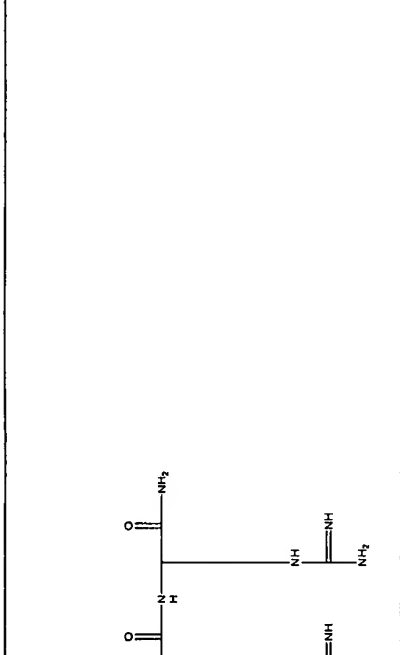
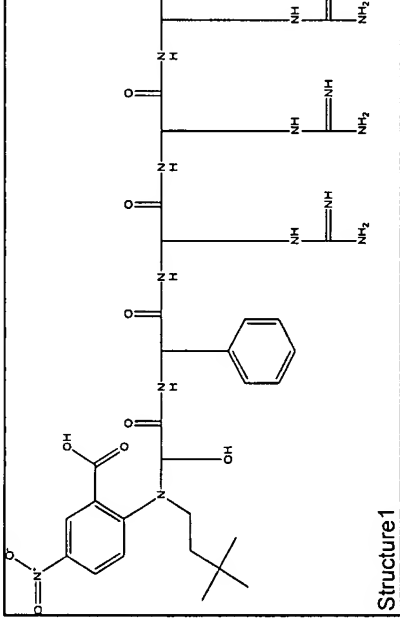
 <p>Structure 1</p>	C50H74N22O15	1223.273	<10%
 <p>Structure 1</p>	C50H72N22O15	1221.2572	<10%
 <p>Structure 1</p>	C50H72N22O16	1237.2566	<10%

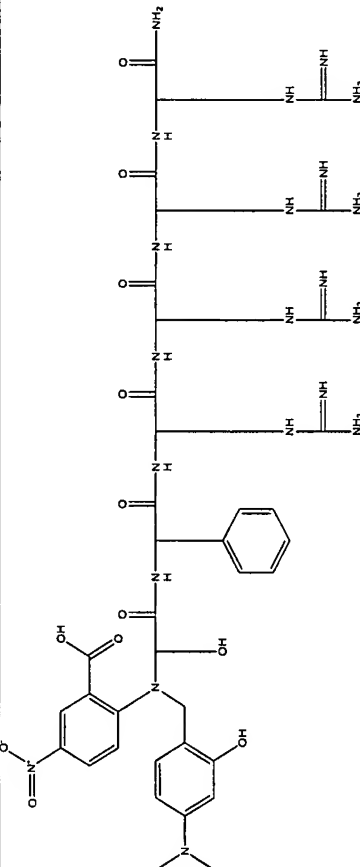
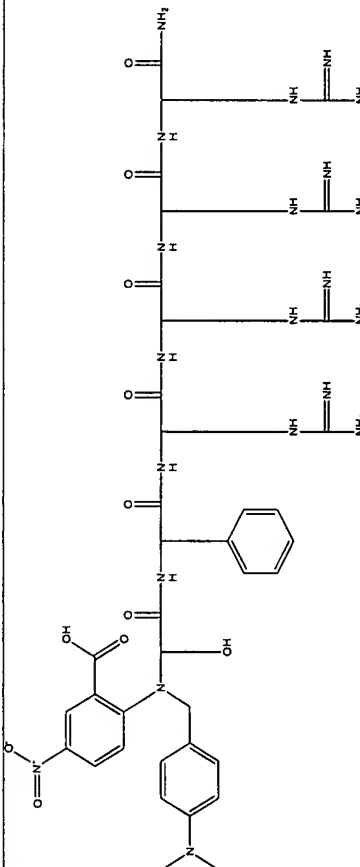
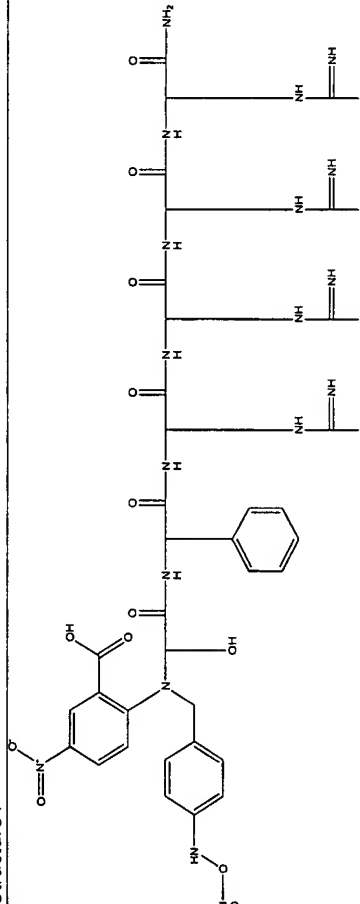
 <p>Structure 1</p>	C52H75N21O13	1202.2974 <10%	
 <p>Structure 1</p>	C54H80N22O13	1245.3656 <10%	
 <p>Structure 1</p>	C52H76N22O15	1249.3108 <10%	

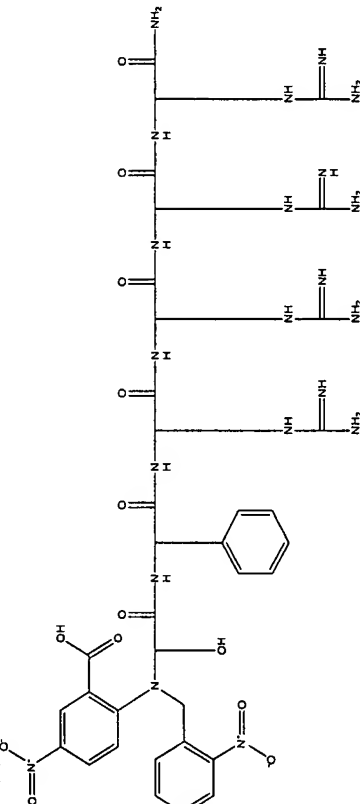
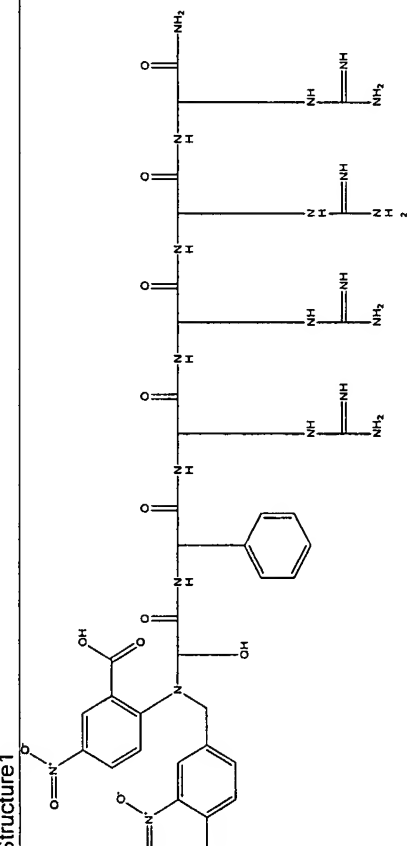
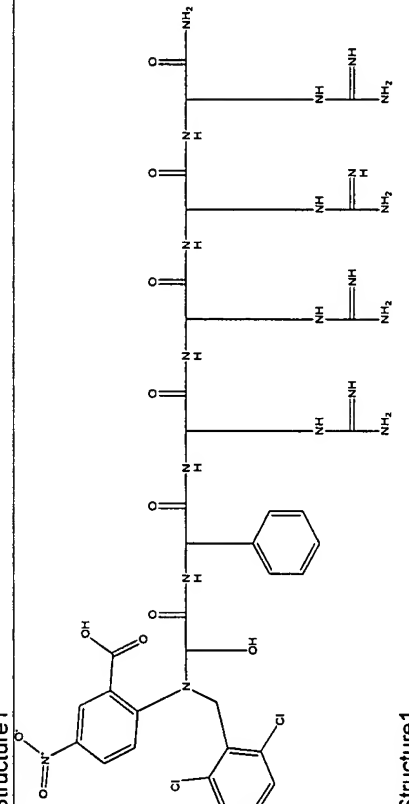
 <p>Structure 1</p>	C58H79N21O13	1278.395 <10%	
 <p>Structure 1</p>	C54H75N21O14	1242.3188 <10%	
 <p>Structure 1</p>	C60H79N21O13	1302.417 <10%	

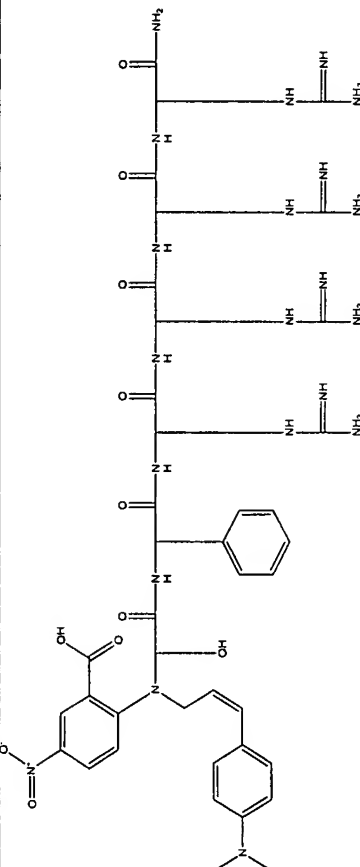
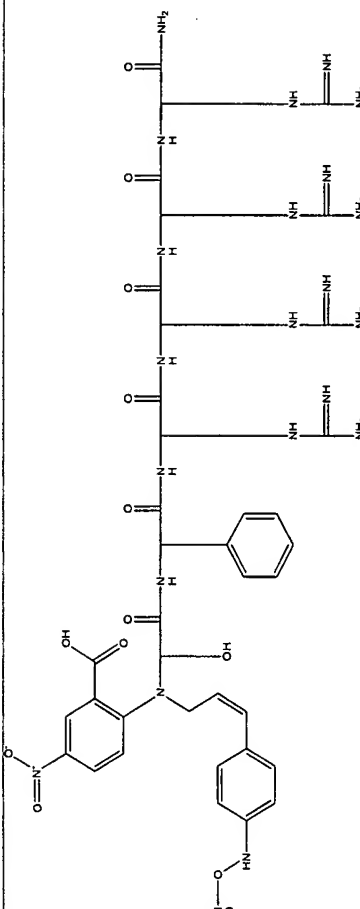
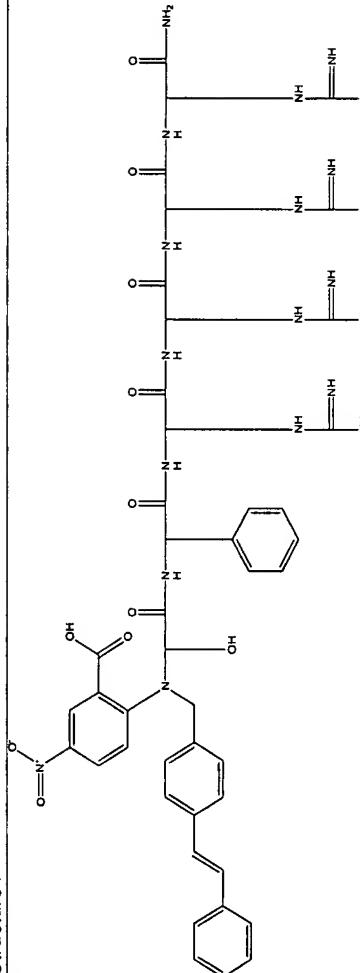
 <p>Structure 1</p>	C58H77N21O13	1276.3792 <10%	
 <p>Structure 1</p>	C58H77N21O13	1276.3792 <10%	
 <p>Structure 1</p>	C51H75N21O14	1206.2858 <10%	

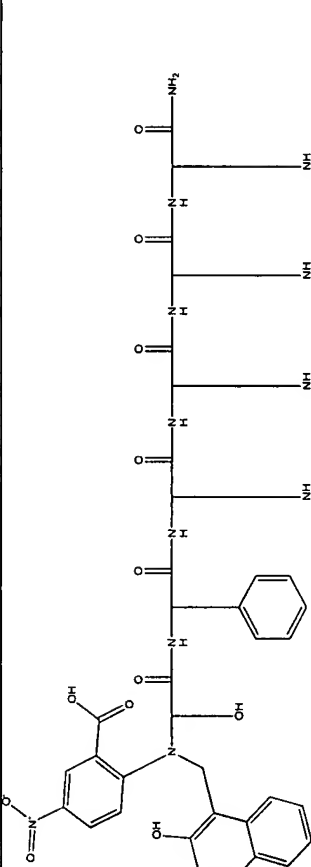
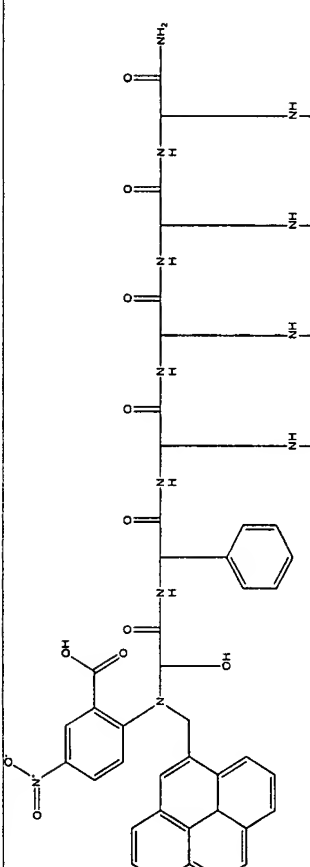
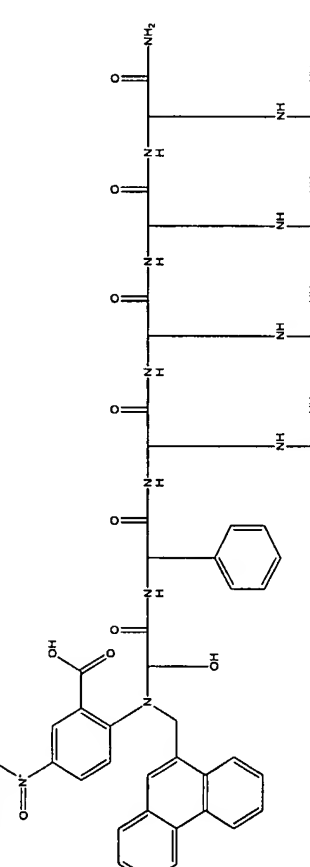
 <p>Structure 1</p>	C51H75N21O15	1222.2852 <10%	
 <p>Structure 1</p>	C46H74N20O11	1083.218 <10%	
 <p>Structure 1</p>	C48H78N20O11	1111.2716 <10%	

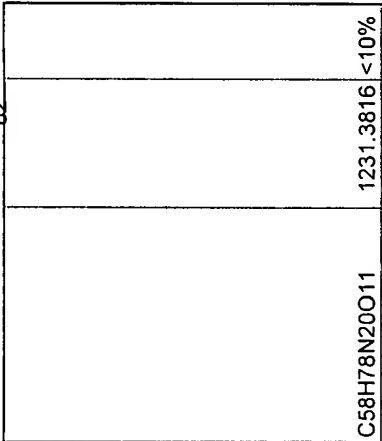
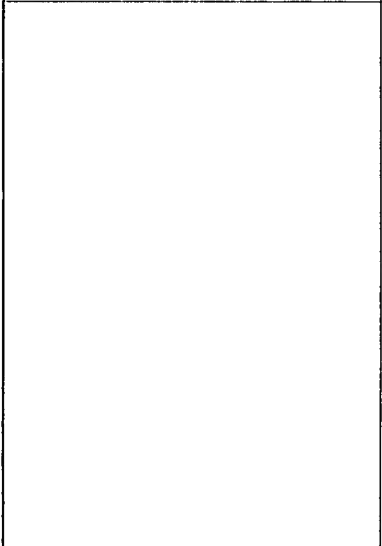
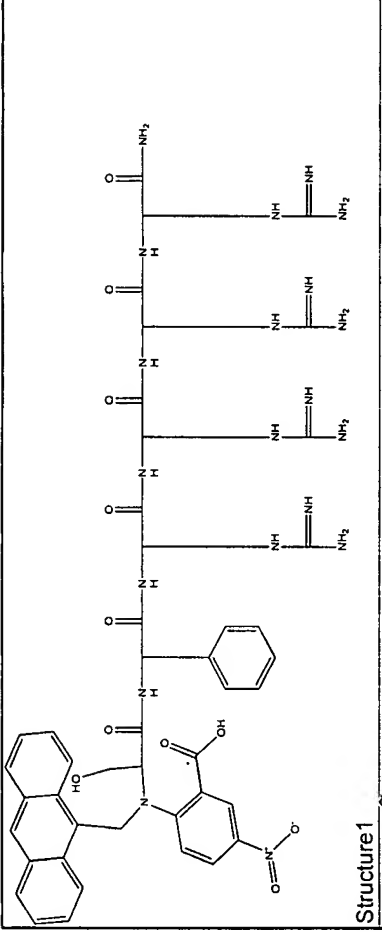
 <p>Structure 1</p>	C49H80N20O11	1125.2984	<10%
 <p>Structure 1</p>	C50H74N20O12	1147.2614	<10%
 <p>Structure 1</p>	C52H78N20O13	1191.3144	<10%

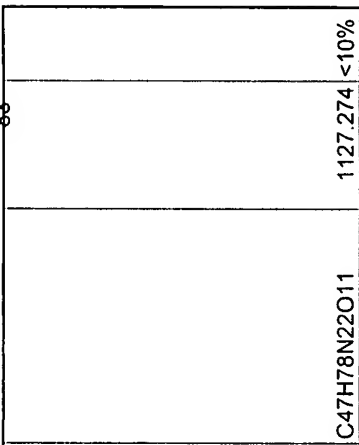
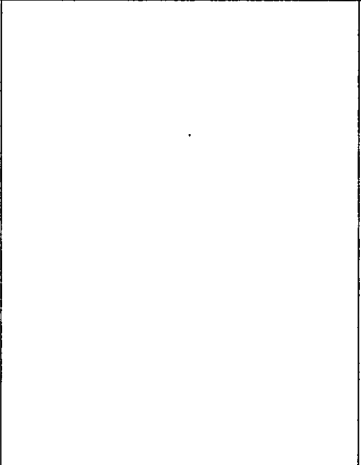
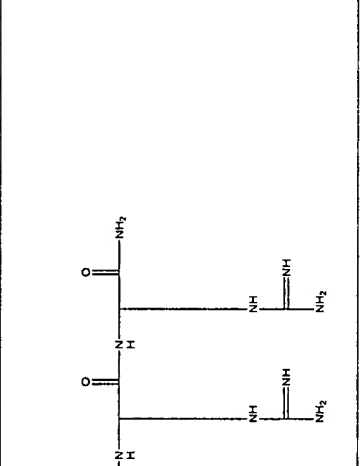
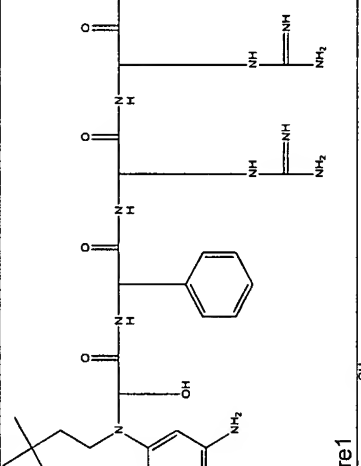
 <p>Structure 1</p>	C52H79N21O12	1190.3296 <10%	
 <p>Structure 1</p>	C52H79N21O11	1174.3302 <10%	
 <p>Structure 1</p>	C50H75N21O13	1178.2754 <10%	

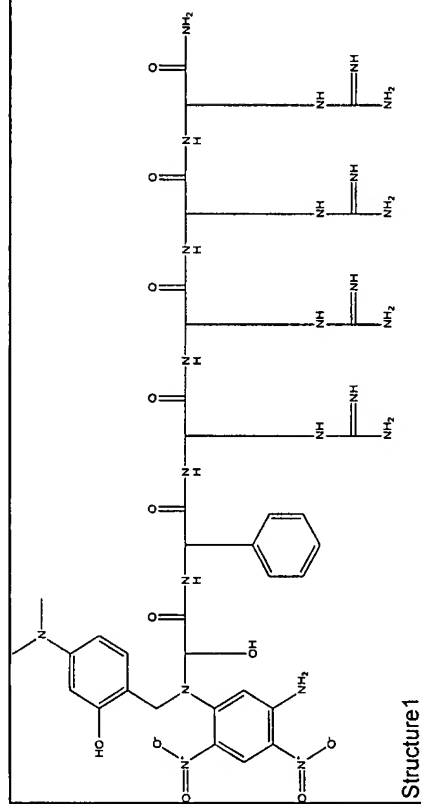
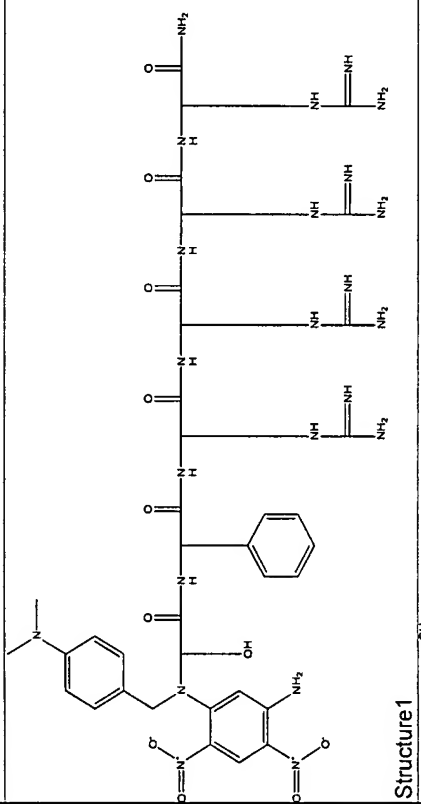
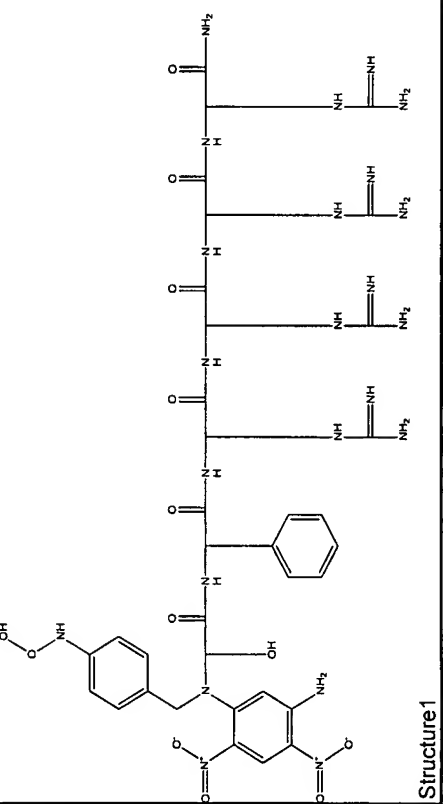
 <p>Structure 1</p>	C50H73N21O13	1176.2596	<10%
 <p>Structure 1</p>	C50H73N21O14	1192.259	<10%
 <p>Structure 1</p>	C50H72Cl2N20O11	1200.1522	<10%

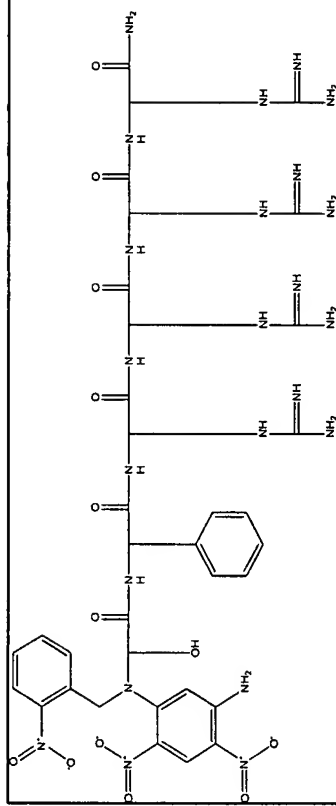
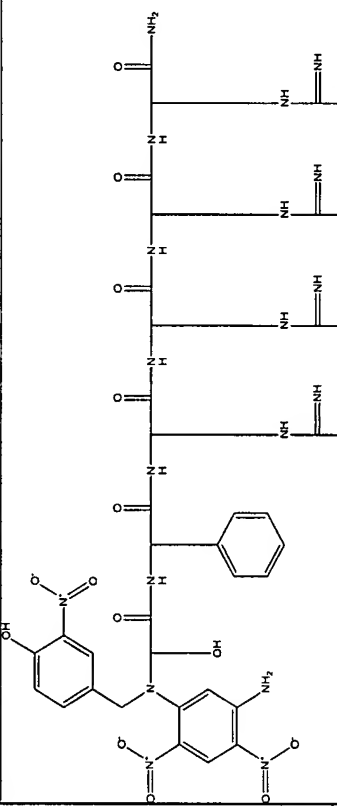
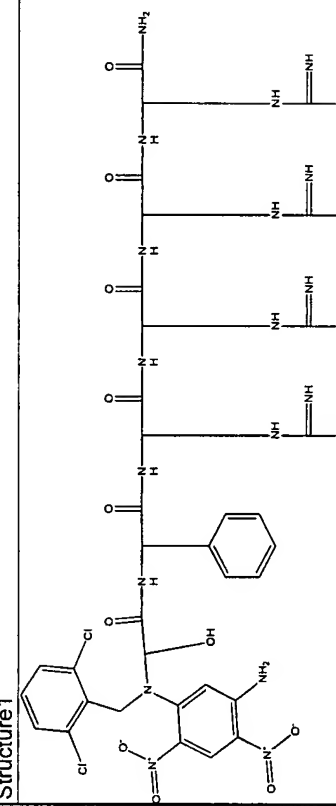
 <p>Structure 1</p>	C54H81N21O11	1200.368	<10%
 <p>Structure 1</p>	C52H77N21O13	1204.3132	<10%
 <p>Structure 1</p>	C58H80N20O11	1233.3974	<10%

 <p>Structure 1</p>	C54H76N20O12	1197.3212 <10%	
 <p>Structure 1</p>	C60H80N20O11	1257.4194 <10%	
 <p>Structure 1</p>	C58H78N20O11	1231.3816 <10%	

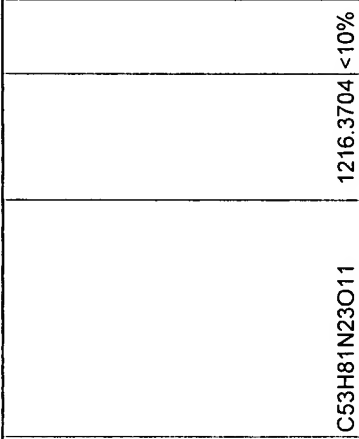
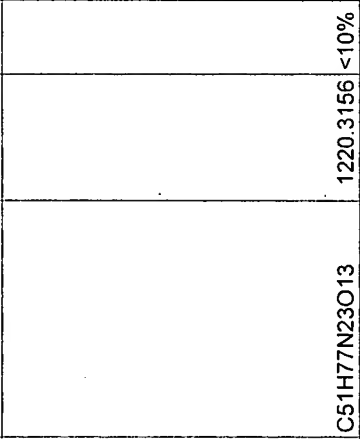
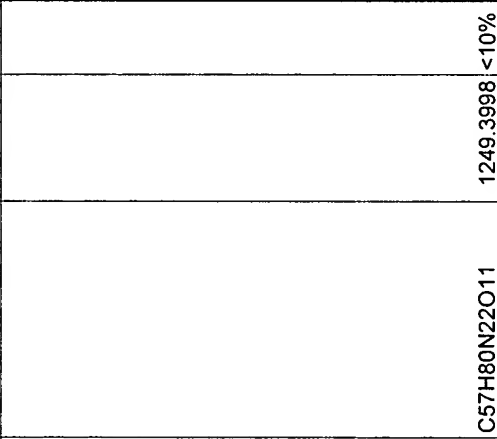
	<p>C58H78N20O11</p> <p>1231.3816 <10%</p>	<p>82</p>	<p>1099.2204 <10%</p>
	<p>C51H76N20O12</p> <p>1161.2882 <10%</p>	<p>1177.2876 <10%</p>	<p>1099.2204 <10%</p>
	<p>C45H74N22O11</p> <p>1099.2204 <10%</p>	<p>1099.2204 <10%</p>	<p>1099.2204 <10%</p>

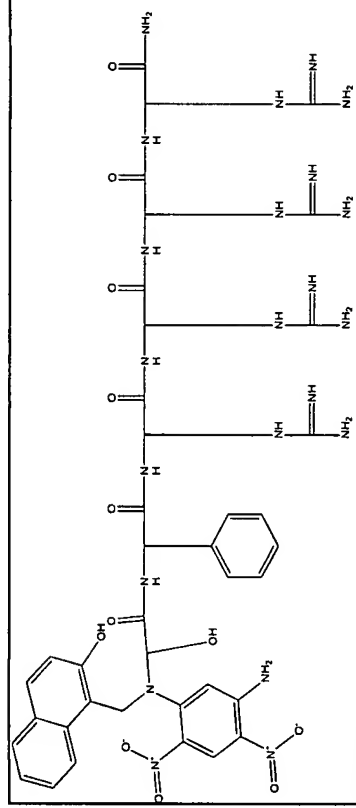
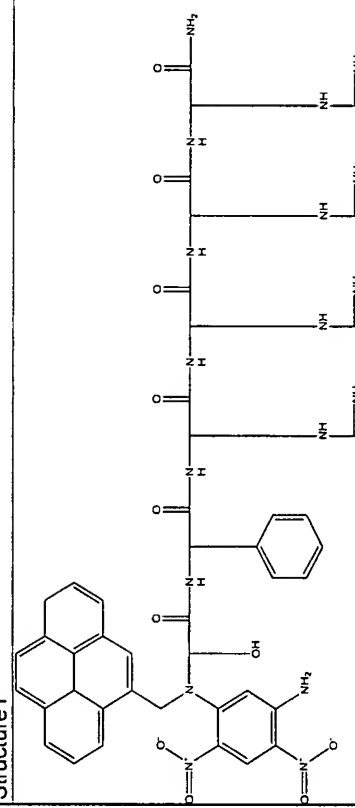
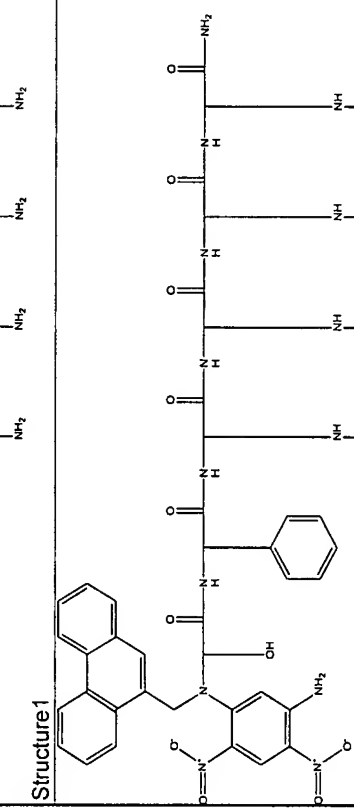
	C47H78N22O11	1127.274 <10%		83
	C48H80N22O11	1141.3008 <10%		
	C49H74N22O12	1163.2638 <10%		
	C51H78N22O13	1207.3168 <10%		

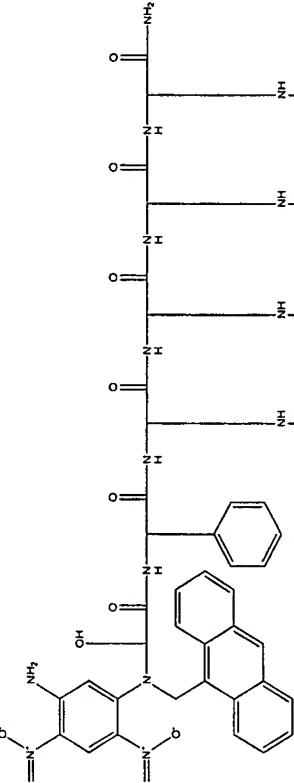
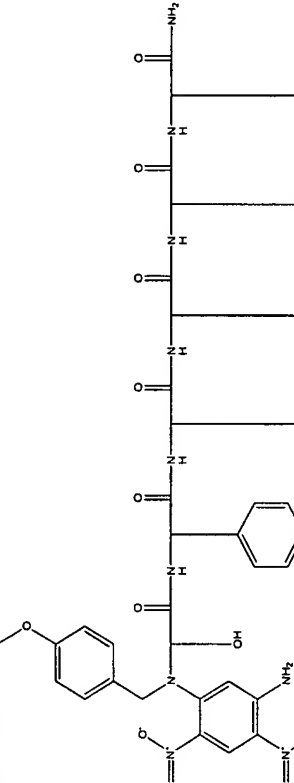
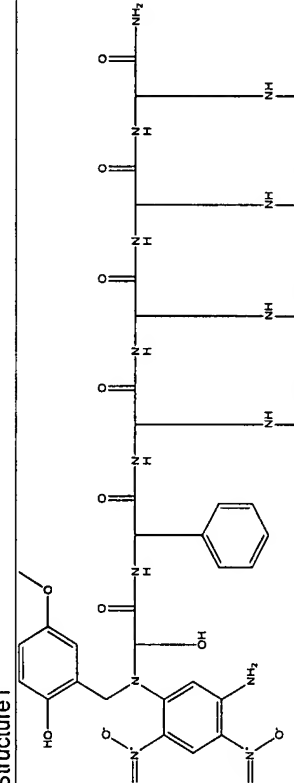
 <p>Structure 1</p>	C51H79N23O12	1206.332	<10%
 <p>Structure 1</p>	C51H79N23O11	1190.3326	<10%
 <p>Structure 1</p>	C49H75N23O13	1194.2778	<10%

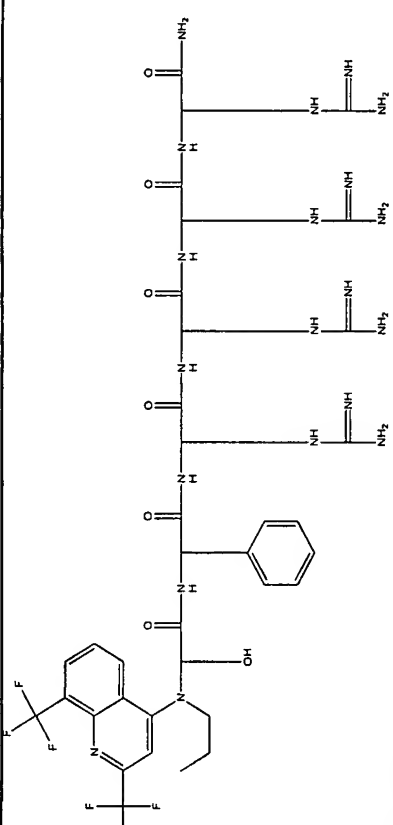
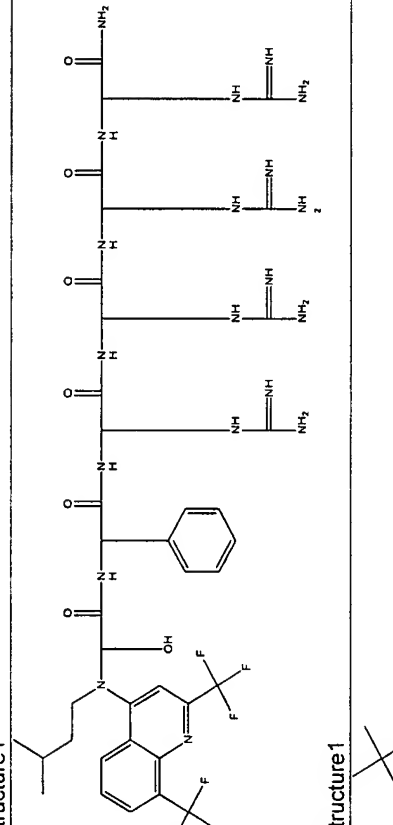
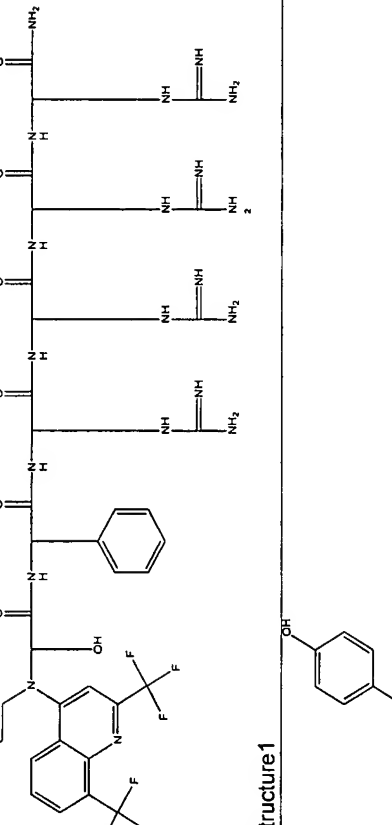
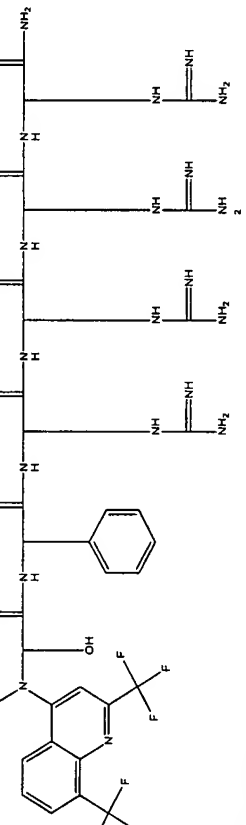
 <p>Structure 1</p>	C49H73N23O13	1192.262	<10%
 <p>Structure 1</p>	C49H73N23O14	1208.2614	<10%
 <p>Structure 1</p>	C49H72Cl2N22O11	1216.1546	<10%

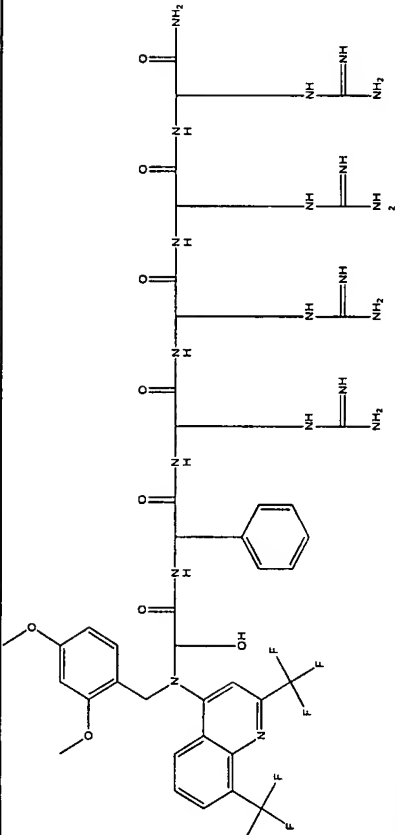
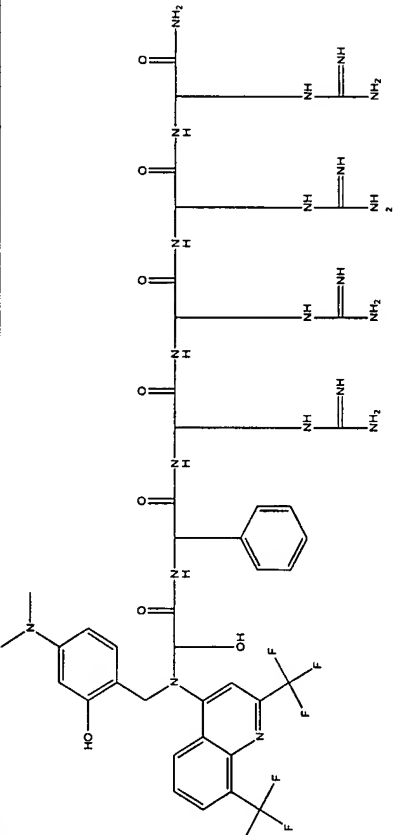
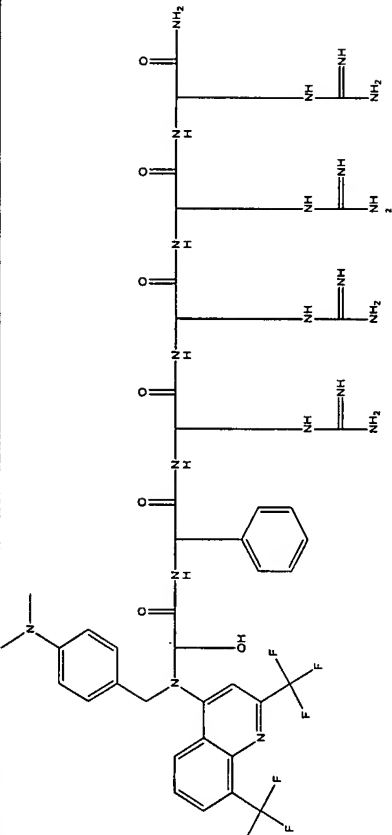
	C49H74N24O15	1239.2754	<10%
	C49H74N24O16	1255.2748	<10%
	C51H76N22O11	1173.3022	<10%

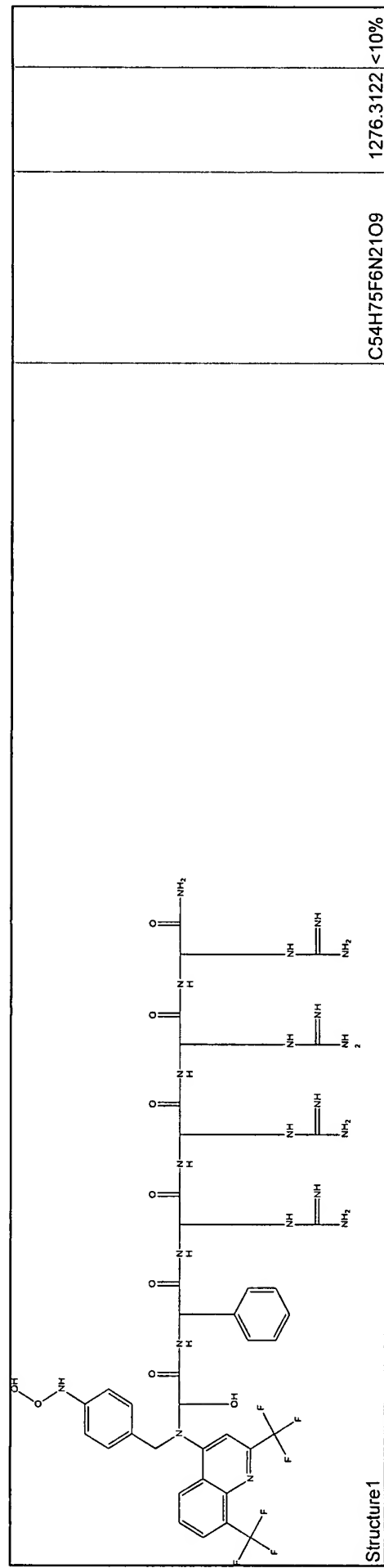
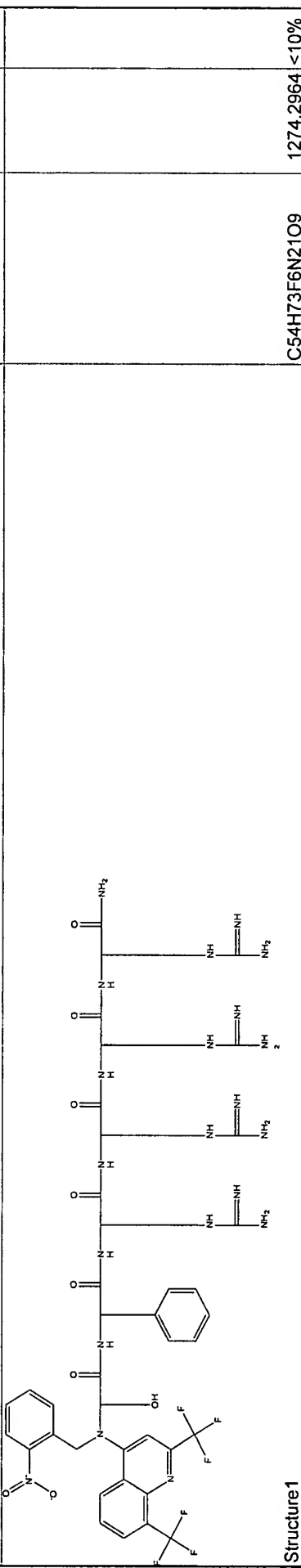
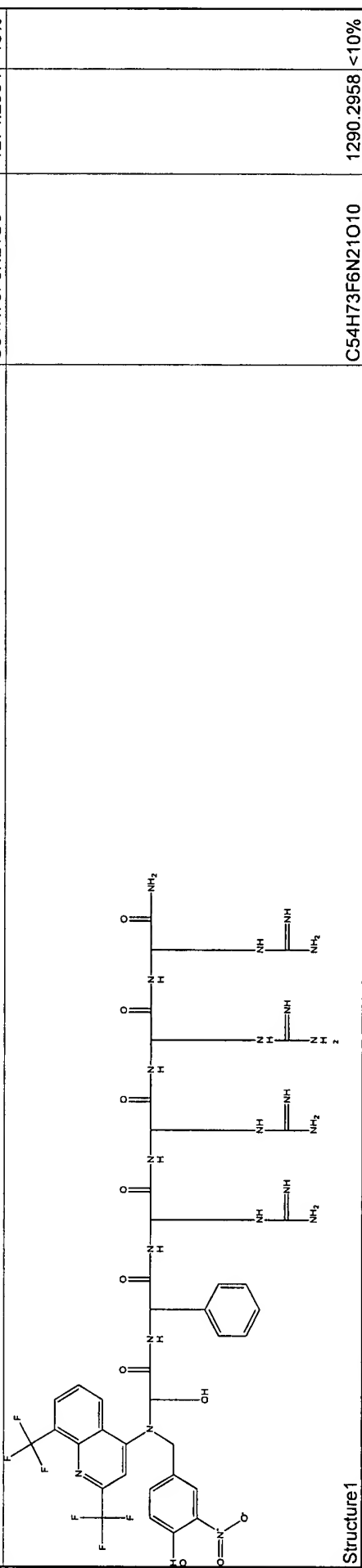
 <p>Chemical structure of C53H81N23O11, a complex molecule featuring a central benzene ring with multiple amide and hydroxyl groups, and a long chain of amide linkages.</p>	C53H81N23O11	1216.3704 <10%	
 <p>Chemical structure of C51H77N23O13, a complex molecule featuring a central benzene ring with multiple amide and hydroxyl groups, and a long chain of amide linkages.</p>	C51H77N23O13	1220.3156 <10%	
 <p>Chemical structure of C57H80N22O11, a complex molecule featuring a central benzene ring with multiple amide and hydroxyl groups, and a long chain of amide linkages.</p>	C57H80N22O11	1249.3998 <10%	

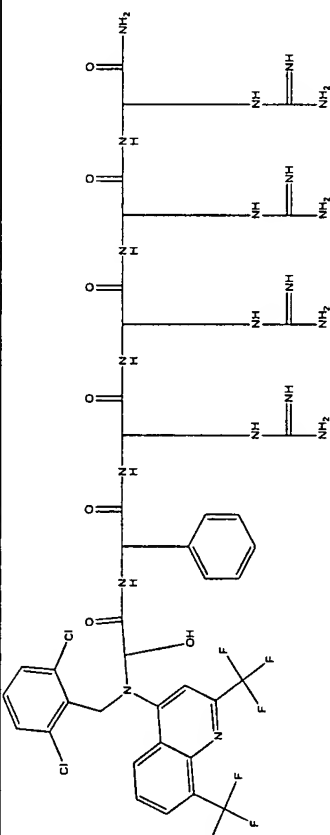
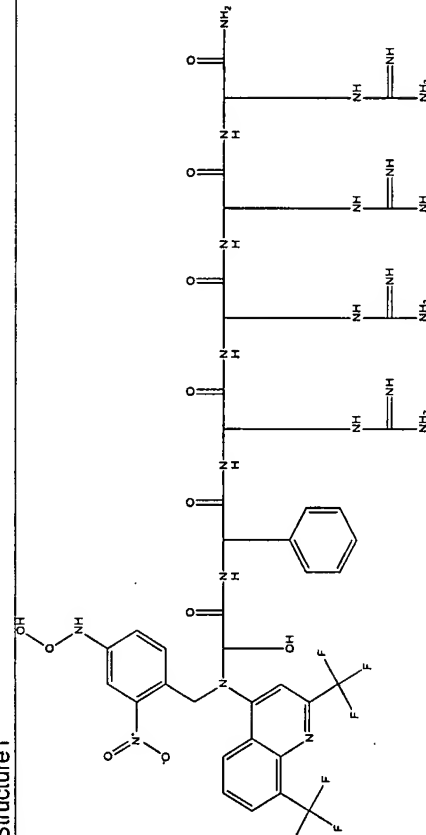
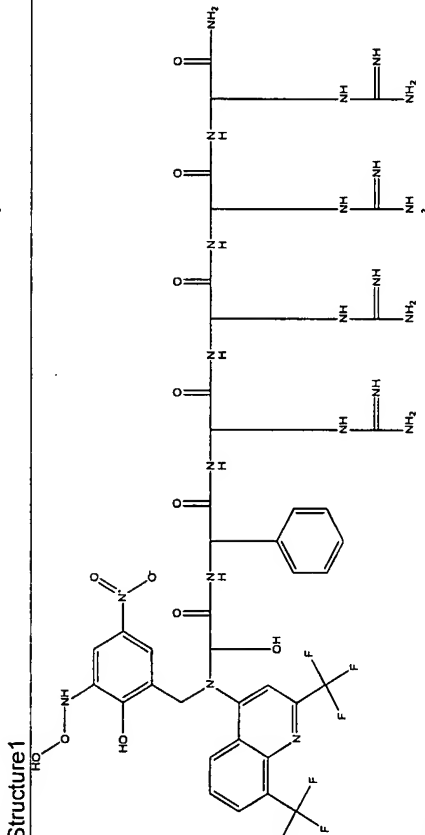
 <p>Structure 1</p>	C53H76N22O12	1213.3236	<10%
 <p>Structure 1</p>	C59H80N22O11	1273.4218	<10%
 <p>Structure 1</p>	C57H78N22O11	1247.384	<10%

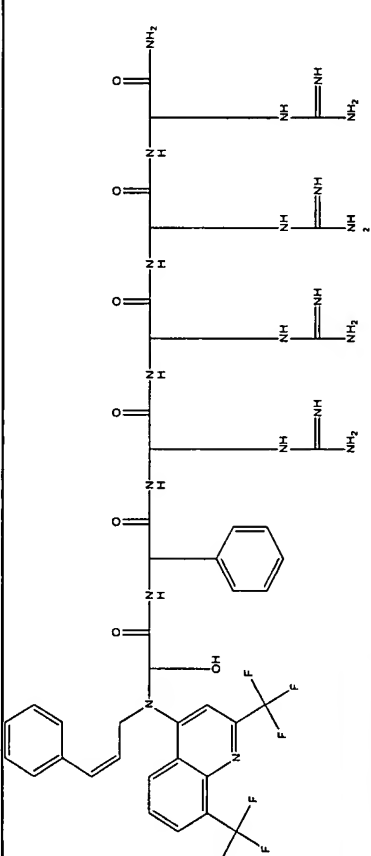
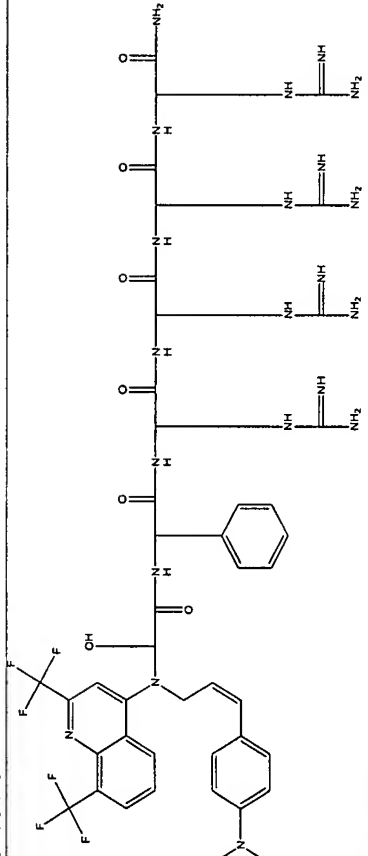
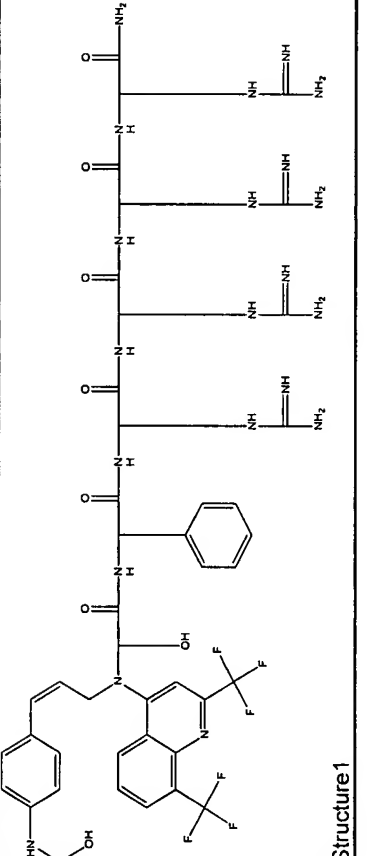
 <p>Structure 1</p>	C57H78N22O11	1247.384	<10%
 <p>Structure 1</p>	C50H76N22O12	1177.2906	<10%
 <p>Structure 1</p>	C50H76N22O13	1193.29	<10%

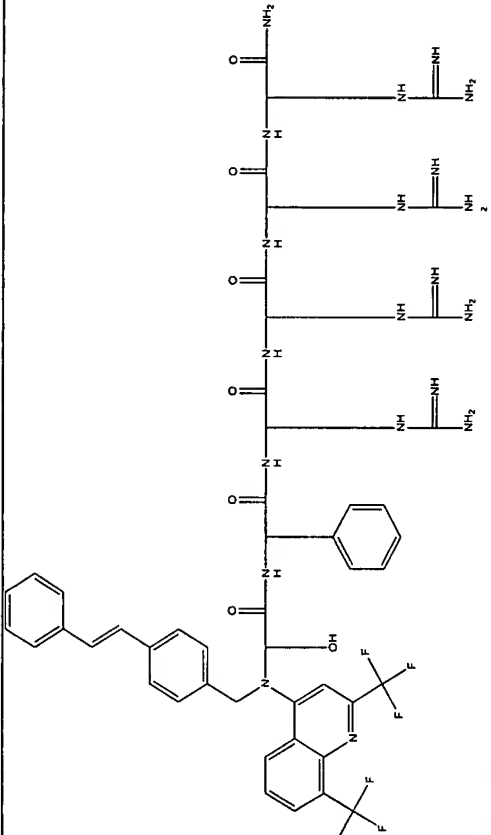
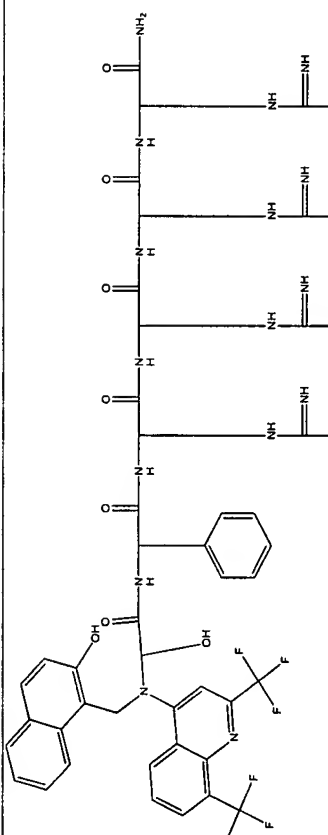
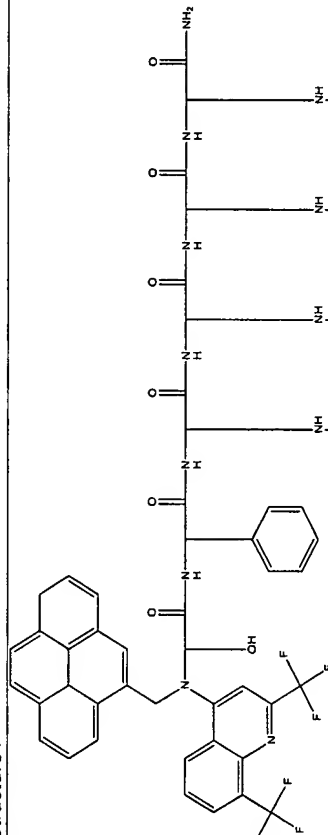
 <p>Structure 1</p>	C50H74F6N2O07	1181.2548 <10%
 <p>Structure 1</p>	C52H78F6N2O07	1209.3084 <10%
 <p>Structure 1</p>	C53H80F6N2O07	1223.3352 <10%
 <p>Structure 1</p>	C54H74F6N2O08	1245.2982 <10%

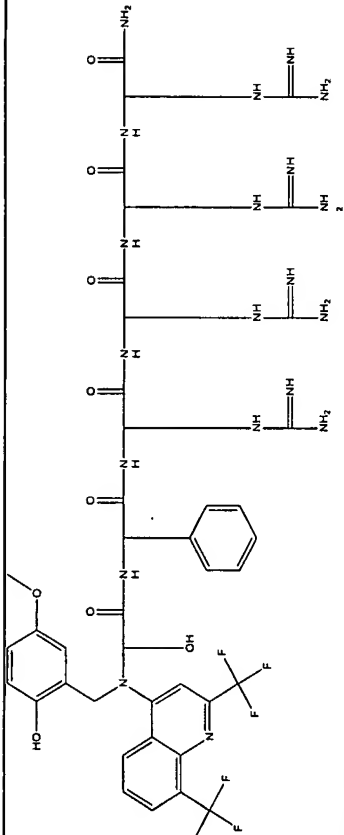
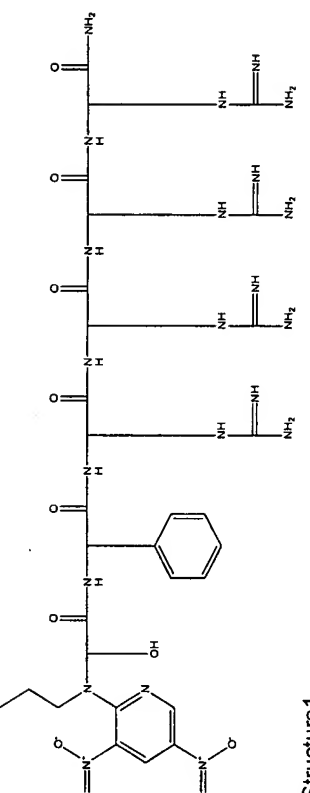
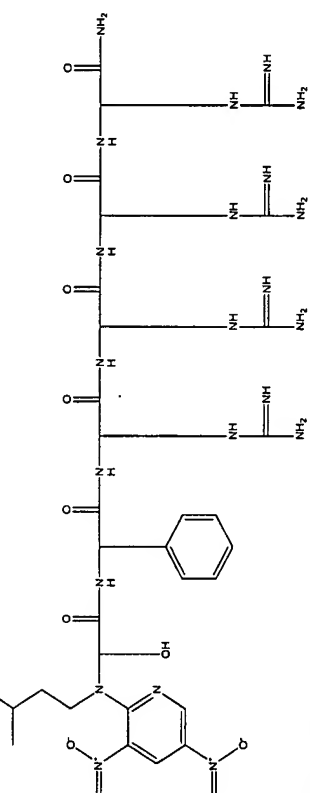
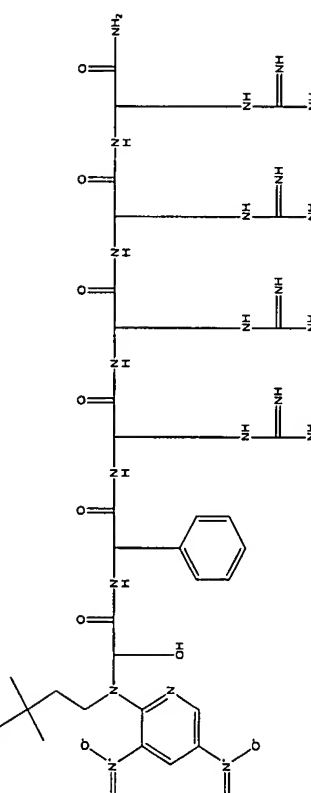
 <p>Structure 1</p>	C56H78F6N2O9	1289.3512	<10%
 <p>Structure 1</p>	C56H79F6N2O8	1288.3664	<10%
 <p>Structure 1</p>	C56H79F6N2O7	1272.367	<10%

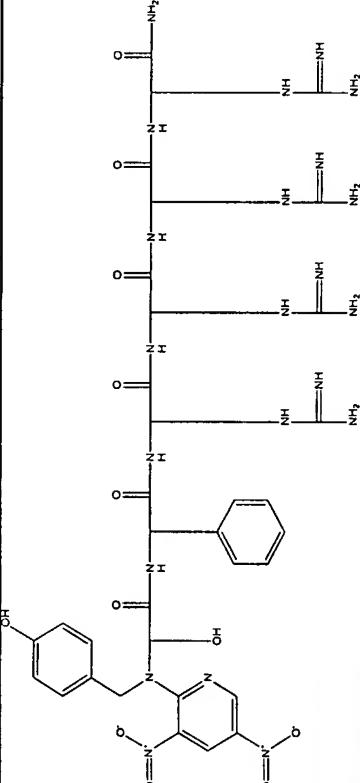
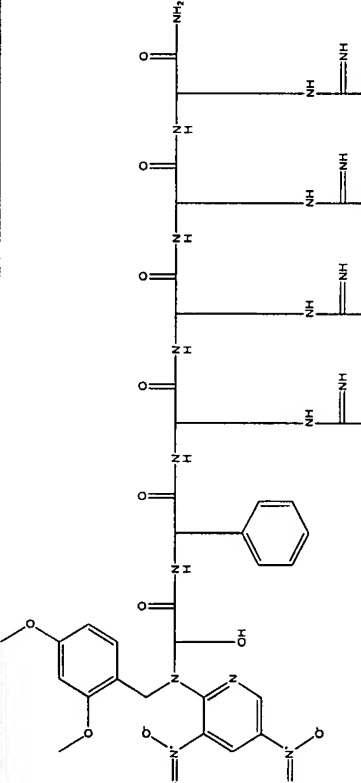
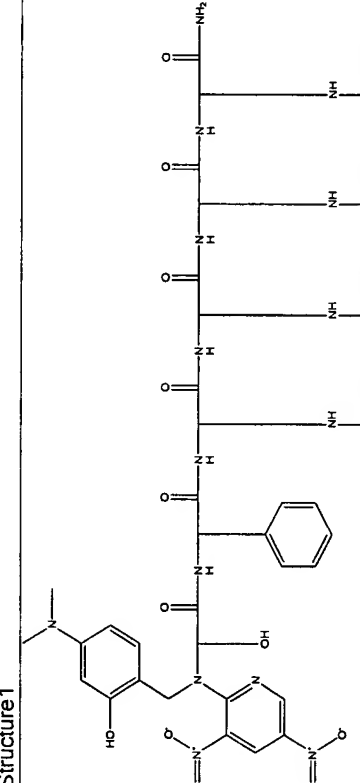
	C54H75F6N2IO9	1276.3122 <10%
	C54H73F6N2IO9	1274.2964 <10%
	C54H73F6N2IO10	1290.2958 <10%

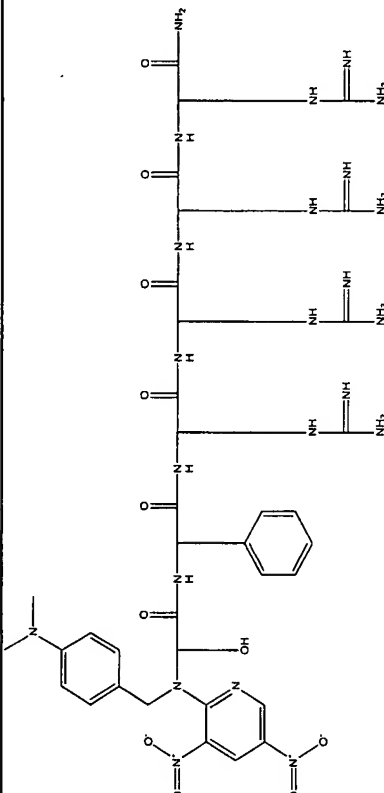
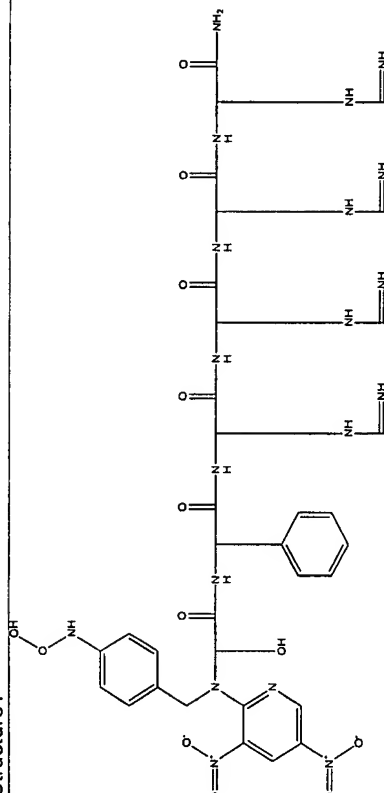
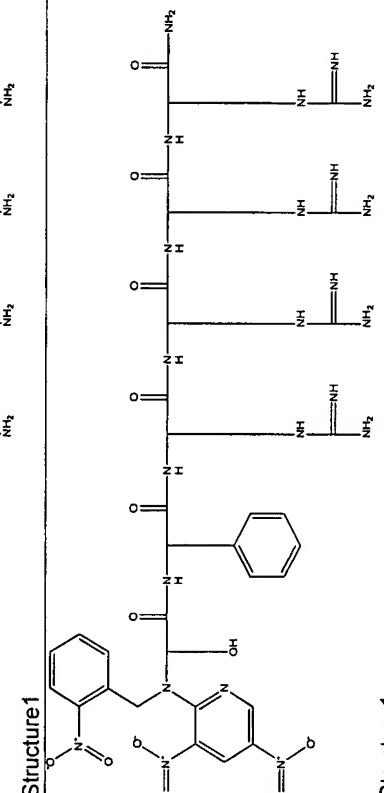
 <p>Structure 1</p>	C54H72Cl2F6N2O7	1298.189	<10%
 <p>Structure 1</p>	C54H74F6N22O11	1321.3098	<10%
 <p>Structure 1</p>	C54H74F6N22O12	1337.3092	<10%

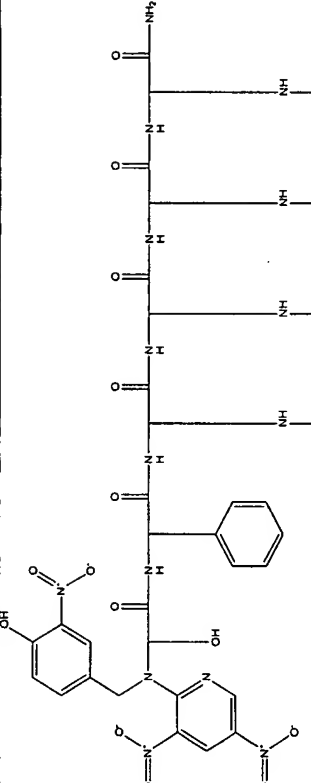
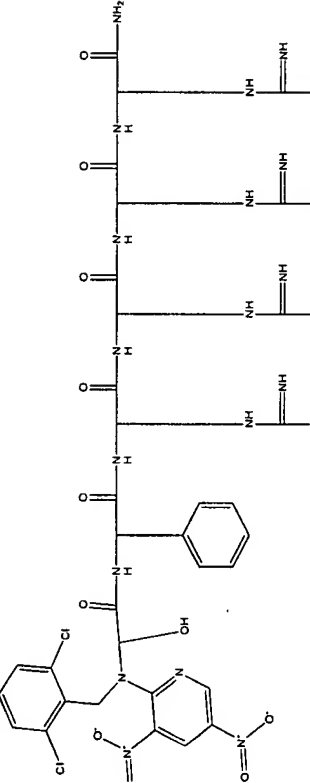
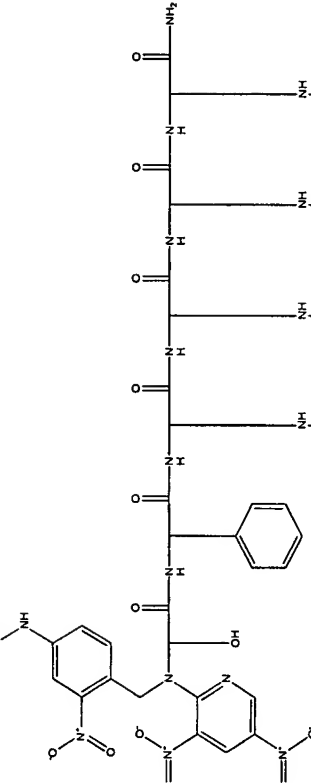
 <p>Structure 1</p>	C56H76F6N2O07	1255.3366	<10%
 <p>Structure 1</p>	C58H81F6N2O07	1298.4048	<10%
 <p>Structure 1</p>	C56H77F6N2O09	1302.35	<10%

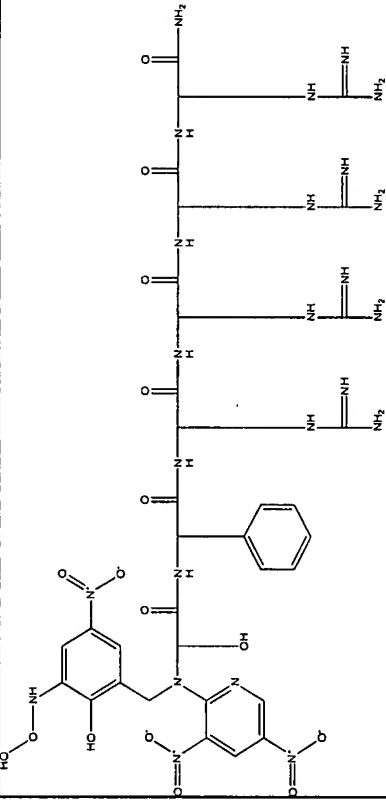
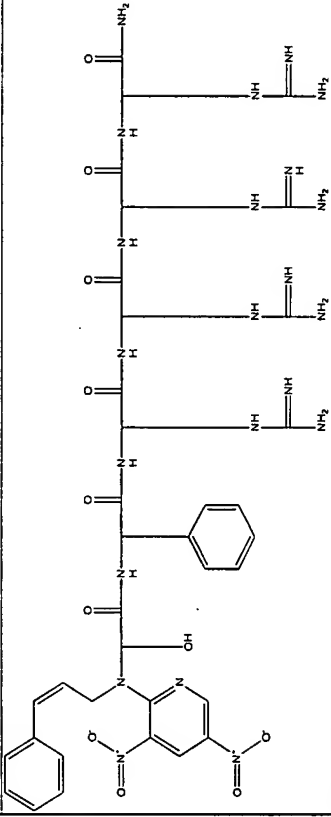
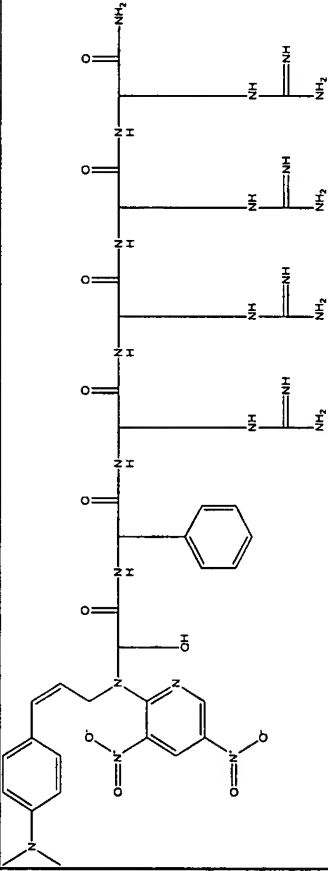
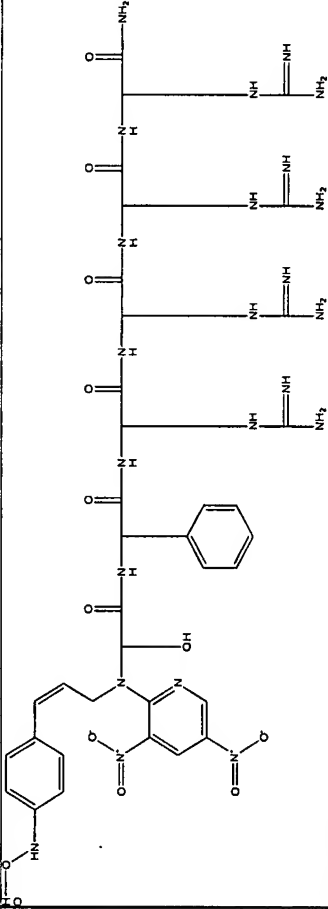
 <p>Structure 1</p>	C62H80F6N20O7	1331.4342 <10%	
 <p>Structure 1</p>	C58H76F6N20O8	1295.358 <10%	
 <p>Structure 1</p>	C64H80F6N20O7	1355.4562 <10%	

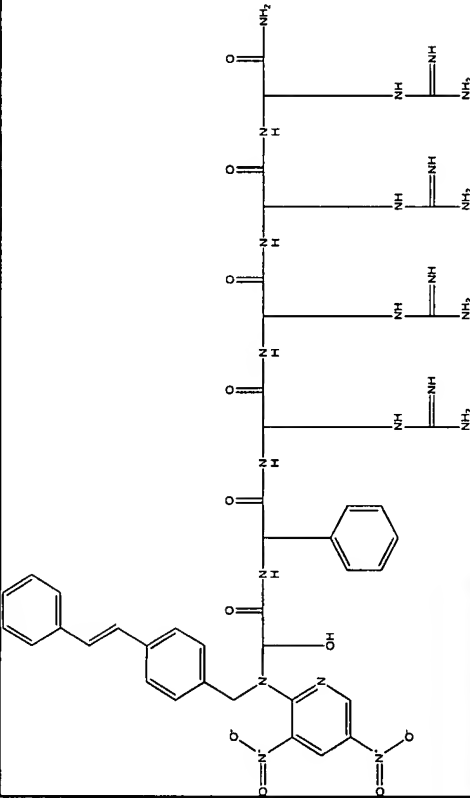
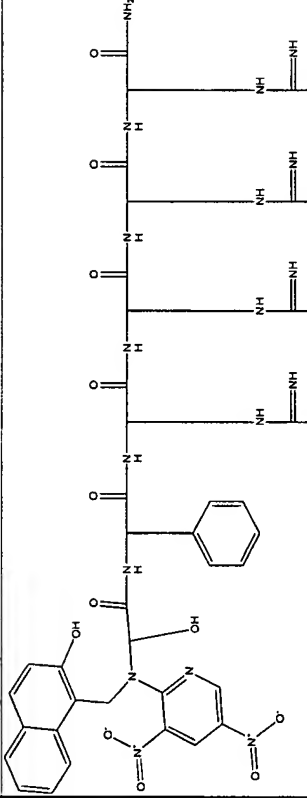
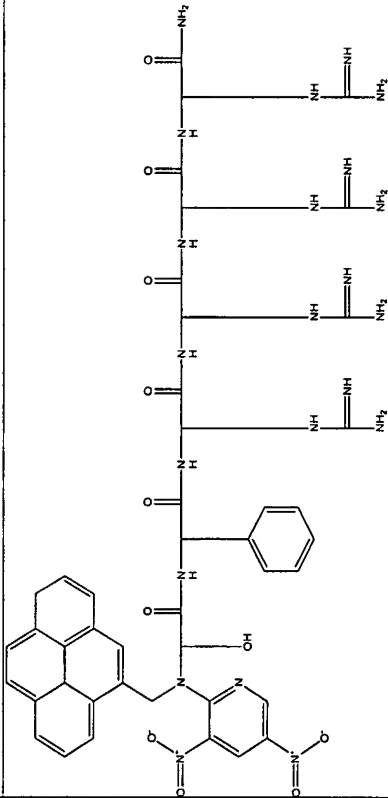
 <p>Structure 1</p>	C55H76F6N20O9	1275.3244 <10%
 <p>Structure 1</p>	C44H72N22O11	1085.1936 <10%
 <p>Structure 1</p>	C46H76N22O11	1113.2472 <10%
 <p>Structure 1</p>	C47H78N22O11	1127.274 <10%

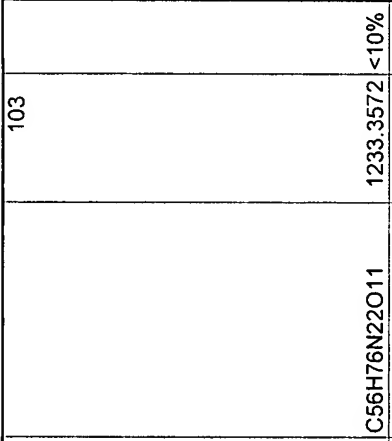
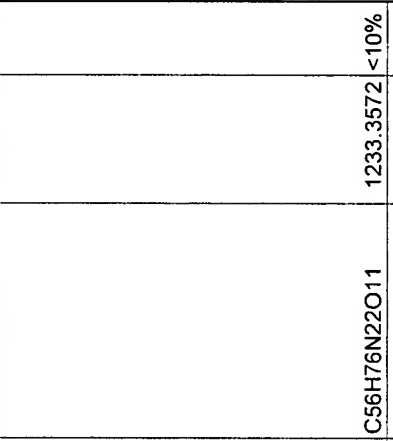
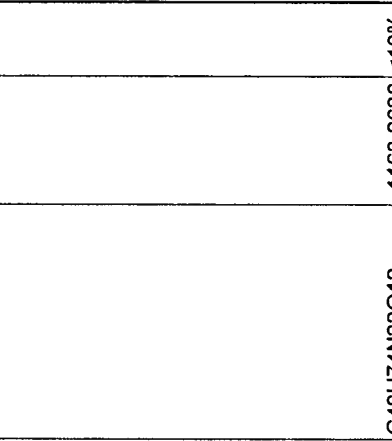
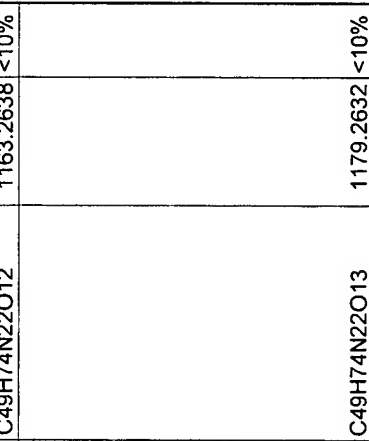
 <p>Structure 1</p>	C48H72N22O12	1149.237	<10%
 <p>Structure 1</p>	C50H76N22O13	1193.29	<10%
 <p>Structure 1</p>	C50H77N23O12	1192.3052	<10%

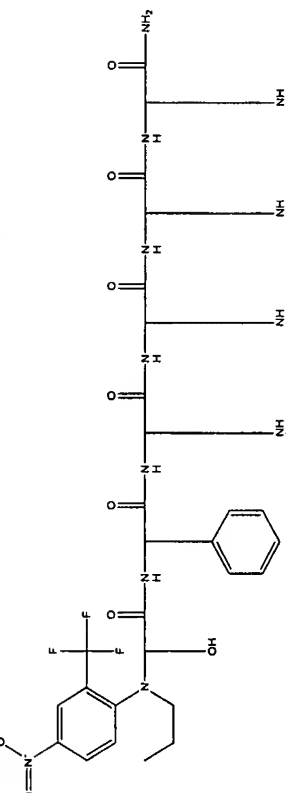
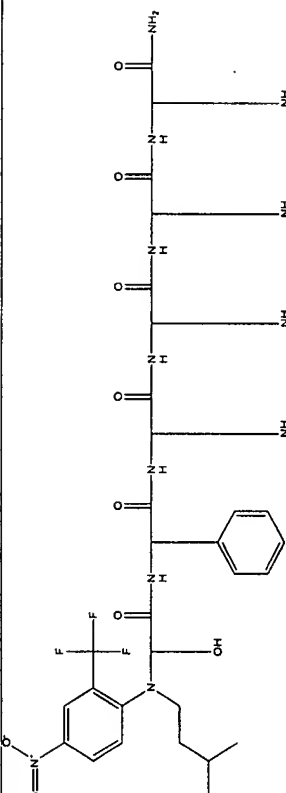
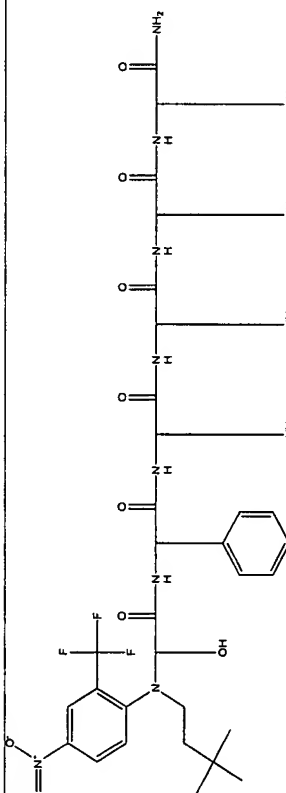
 <p>Structure 1</p>	C50H77N23O11	1176.3058	<10%
 <p>Structure 1</p>	C48H73N23O13	1180.251	<10%
 <p>Structure 1</p>	C48H71N23O13	1178.2352	<10%

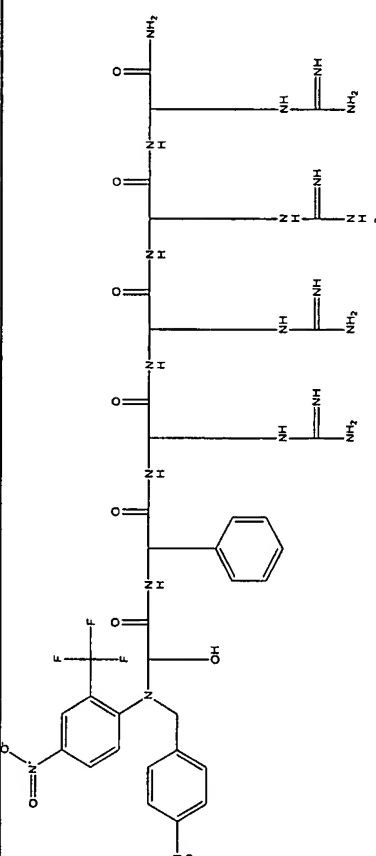
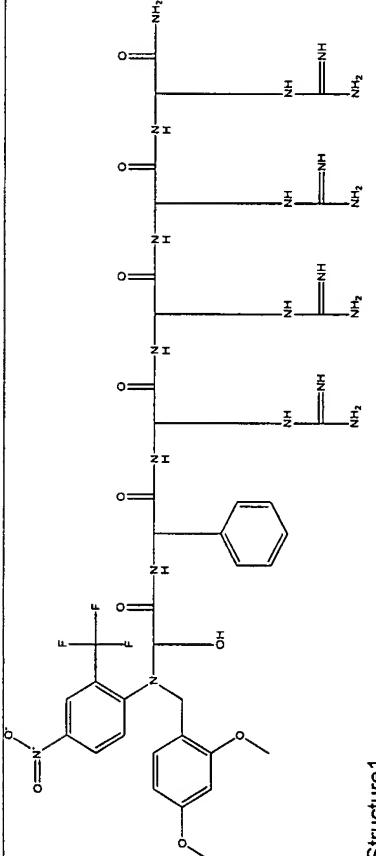
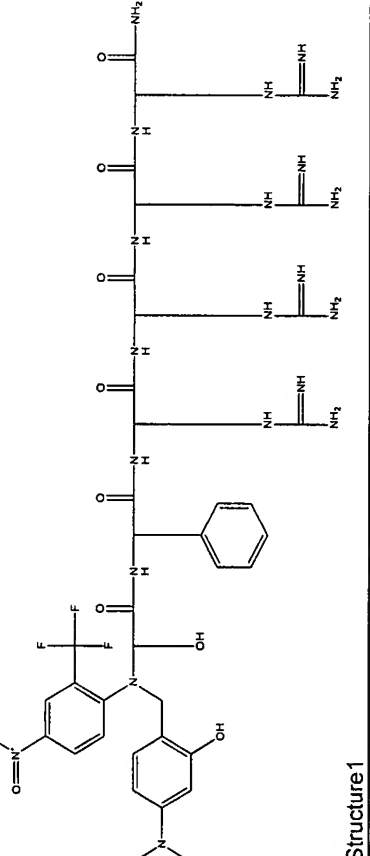
 <p>Structure 1</p>	C48H71N23O14	1194.2346	<10%
 <p>Structure 1</p>	C48H70Cl2N22O11	1202.1278	<10%
 <p>Structure 1</p>	C48H72N24O15	1225.2486	<10%

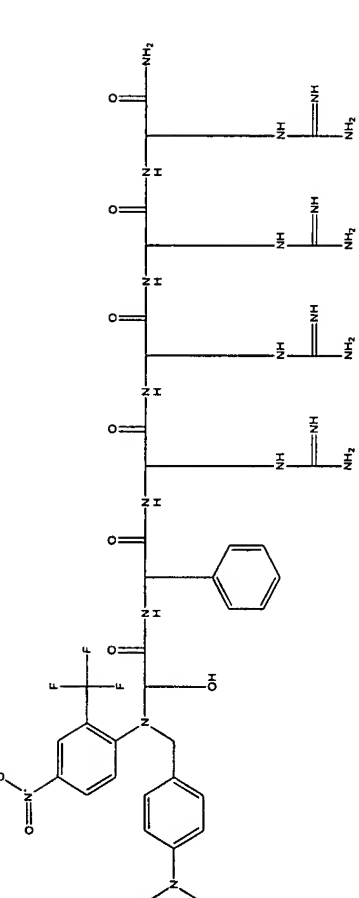
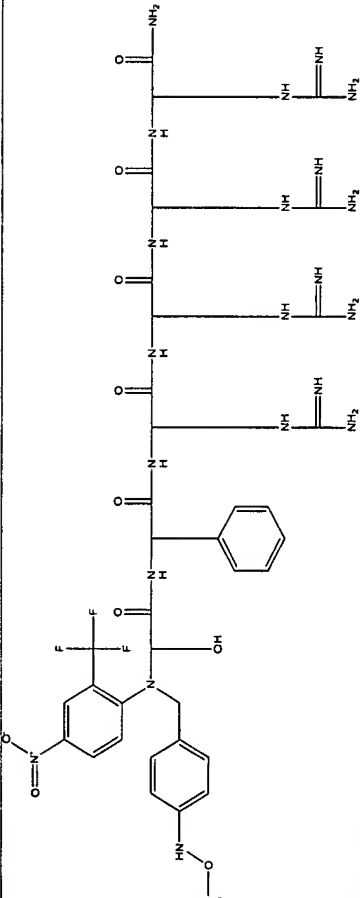
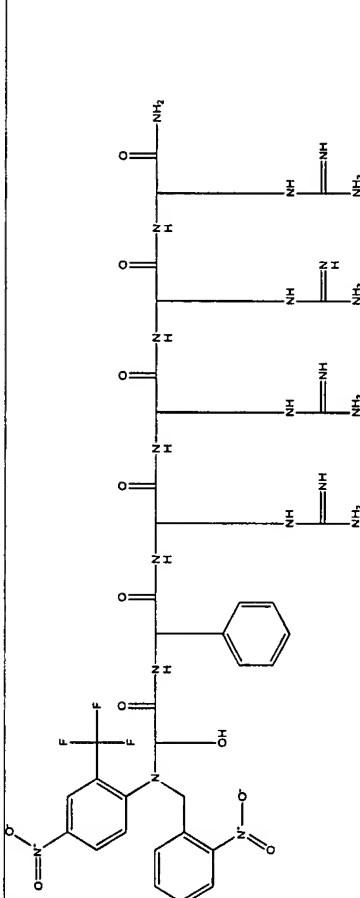
 <p>Structure 1</p>	C48H72N24O16	1241.248 <10%
 <p>Structure 1</p>	C50H74N22O11	1159.2754 <10%
 <p>Structure 1</p>	C52H79N23O11	1202.3436 <10%
 <p>Structure 1</p>	C50H75N23O13	1206.2888 <10%

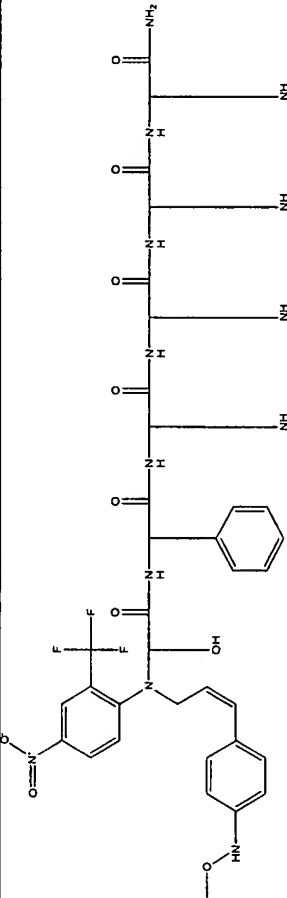
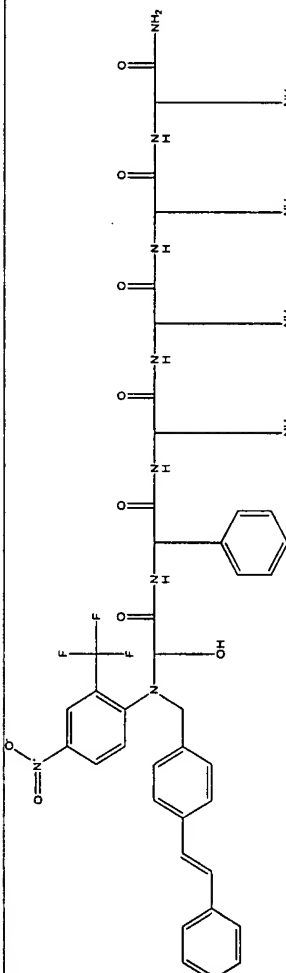
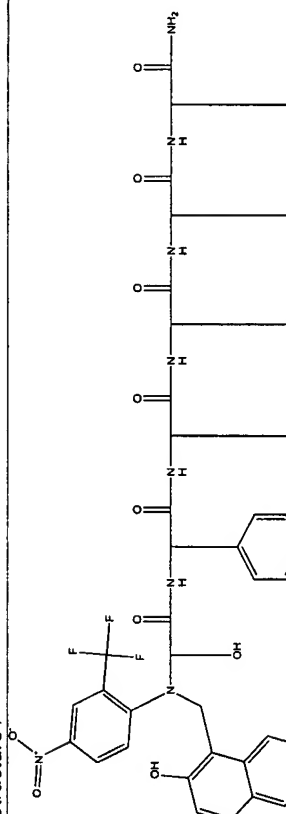
 <p>Structure 1</p>	C56H78N22O11	1235.373 <10%	
 <p>Structure 1</p>	C52H74N22O12	1199.2968 <10%	
 <p>Structure 1</p>	C58H78N22O11	1259.395 <10%	

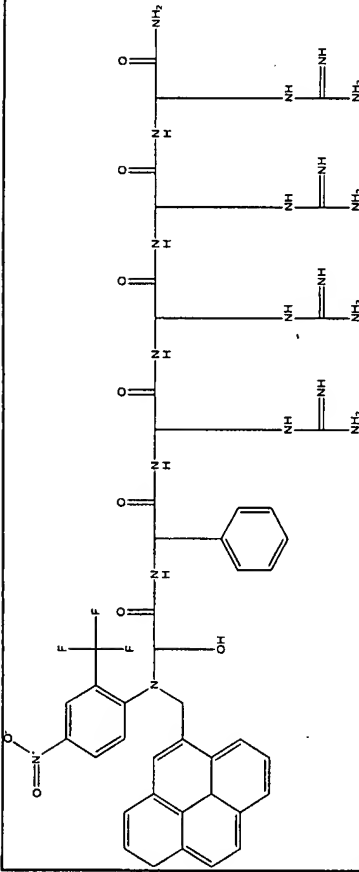
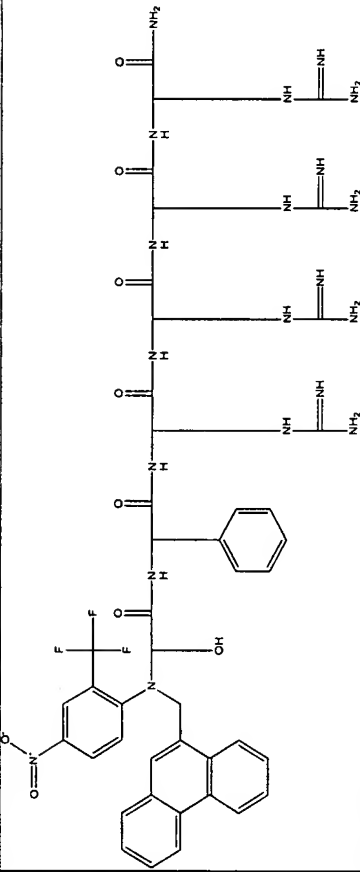
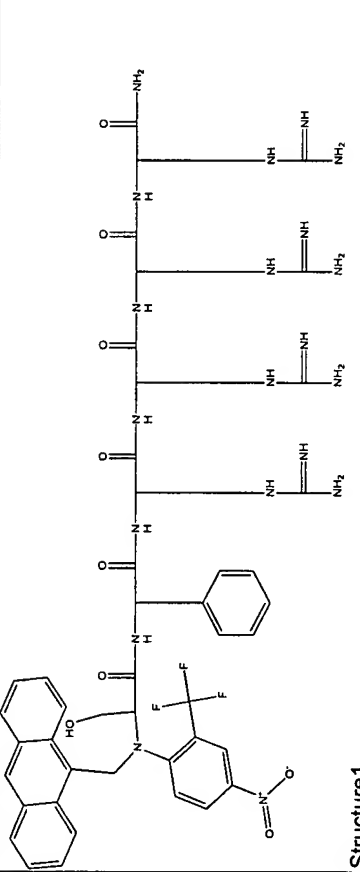
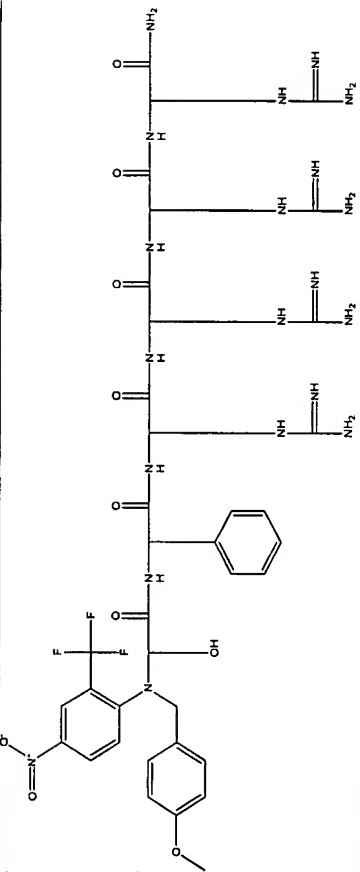
 <p>Structure 1</p>	C56H76N22O11	1233.3572 <10%	103
 <p>Structure 1</p>	C56H76N22O11	1233.3572 <10%	
 <p>Structure 1</p>	C49H74N22O12	1163.2638 <10%	
 <p>Structure 1</p>	C49H74N22O13	1179.2632 <10%	

 Structure 1	C46H73F3N20O9	1107.2065	<10%
 Structure 1	C48H77F3N20O9	1135.2601	<10%
 Structure 1	C49H79F3N20O9	1149.2869	<10%

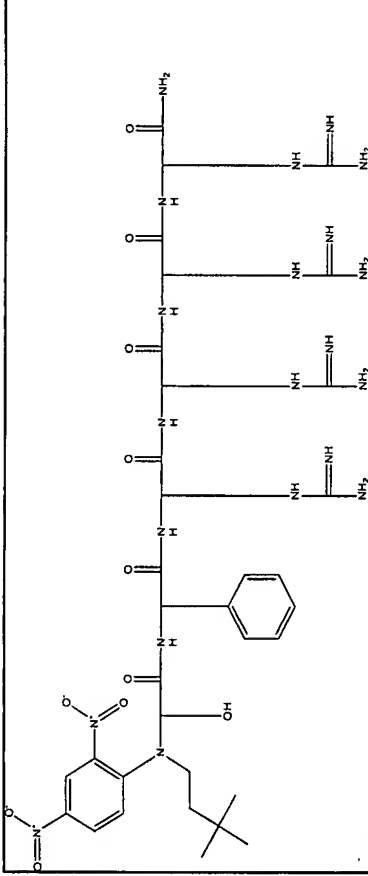
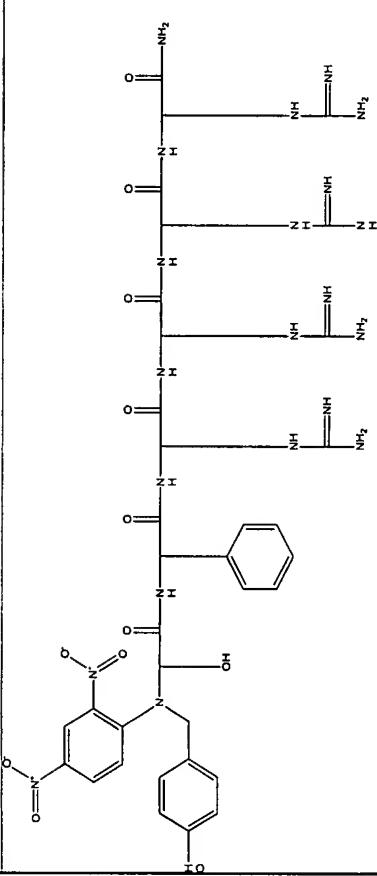
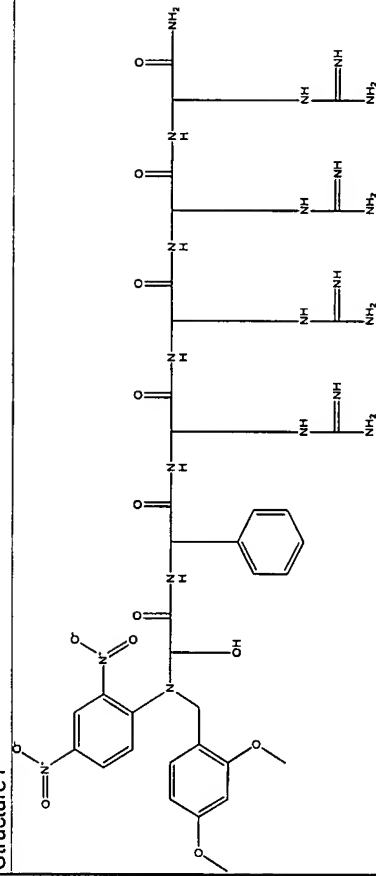
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 <p>Structure 1</p>	C52H77F3N2O11	1215.3029	<10%
 <p>Structure 1</p>	C52H78F3N2O10	1214.3181	<10%

 <p>Structure 1</p>	C52H78F3N21O9	1198.3187	<10%
 <p>Structure 1</p>	C50H74F3N21O11	1202.2639	<10%
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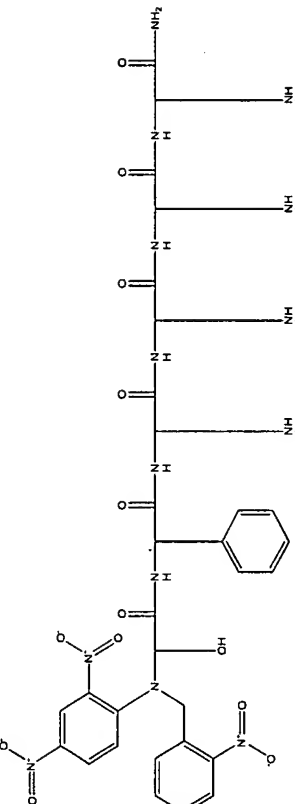
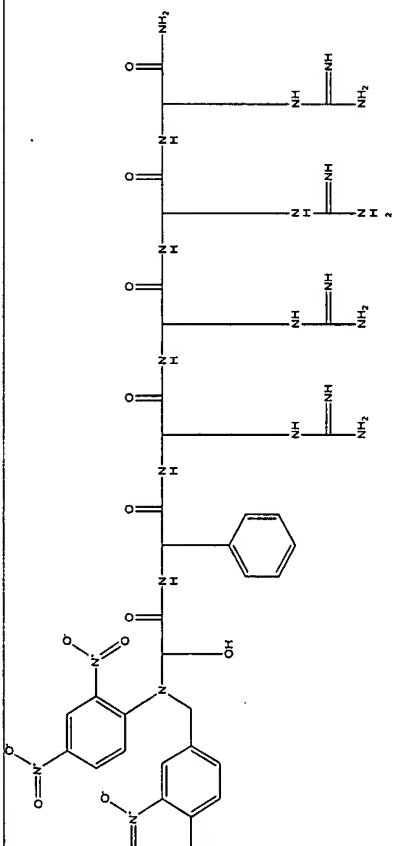
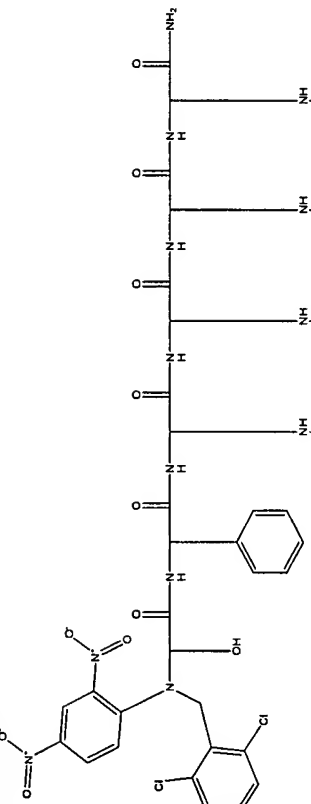
 <p>Structure 1</p>	C52H76F3N2O11	1228.3017	<10%
 <p>Structure 1</p>	C58H79F3N2O09	1257.3859	<10%
 <p>Structure 1</p>	C54H75F3N2O010	1221.3097	<10%

 <p>Structure 1</p>	C60H79F3N20O9	1281.4079 <10%	110
 <p>Structure 1</p>	C58H77F3N20O9	1255.3701 <10%	
 <p>Structure 1</p>	C58H77F3N20O9	1255.3701 <10%	
 <p>Structure 1</p>	C51H75F3N20O10	1185.2767 <10%	

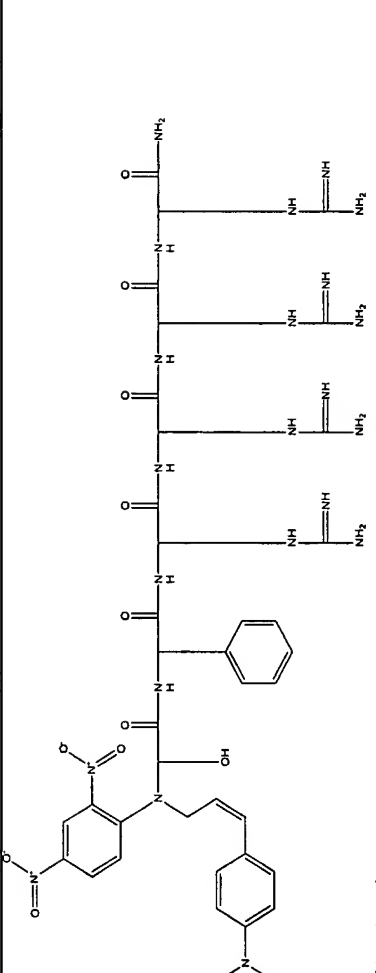
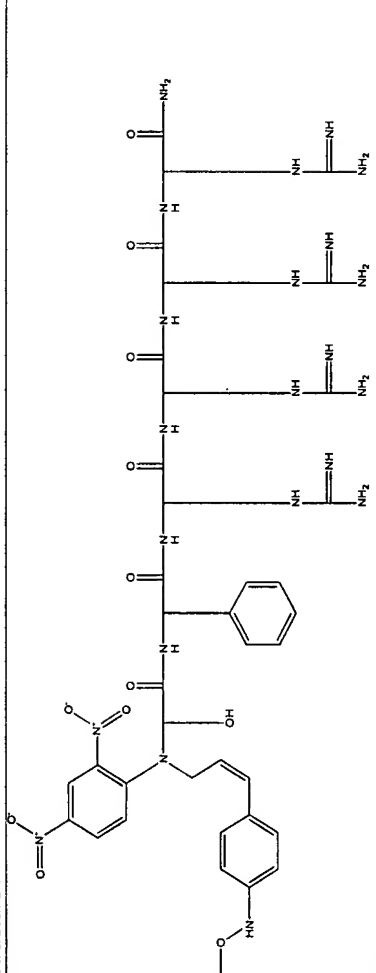
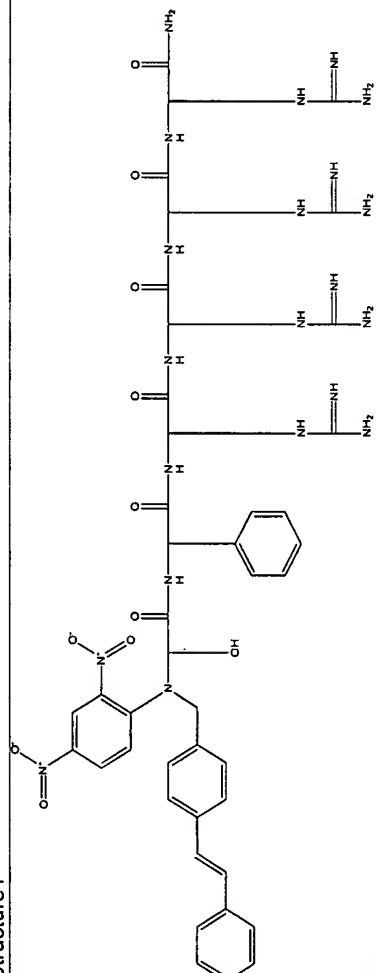
	C51H75F3N2O11	1201.2761	<10%
	C45H73N21O11	1084.2058	<10%
	C47H77N21O11	1112.2594	<10%

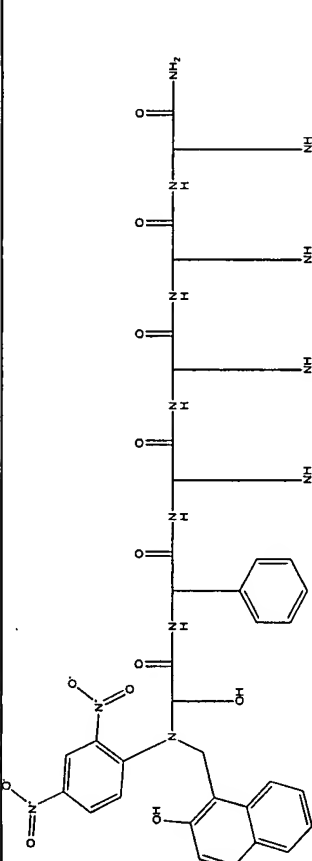
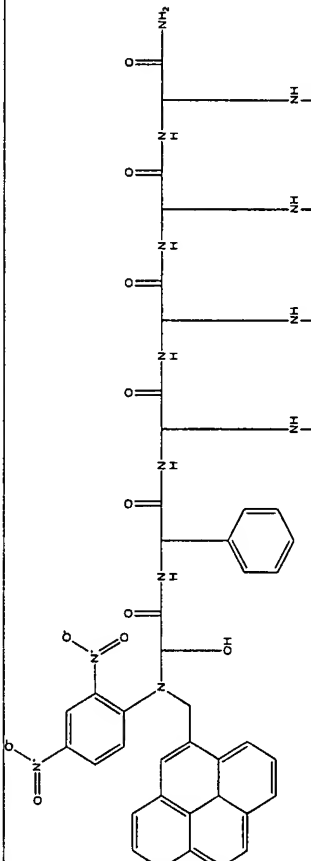
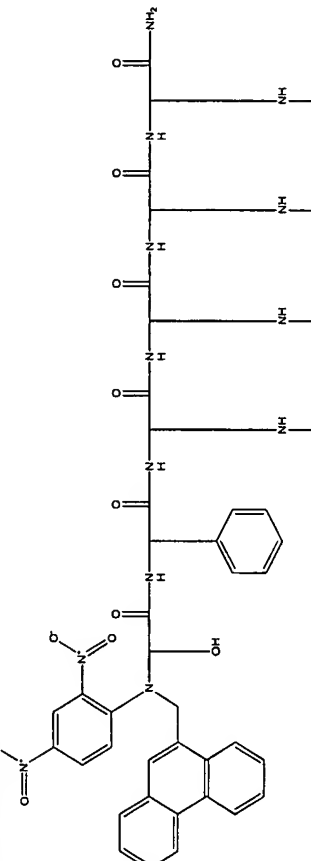
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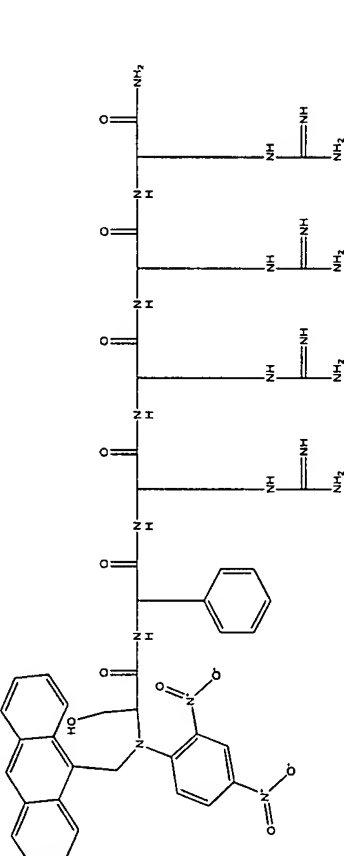
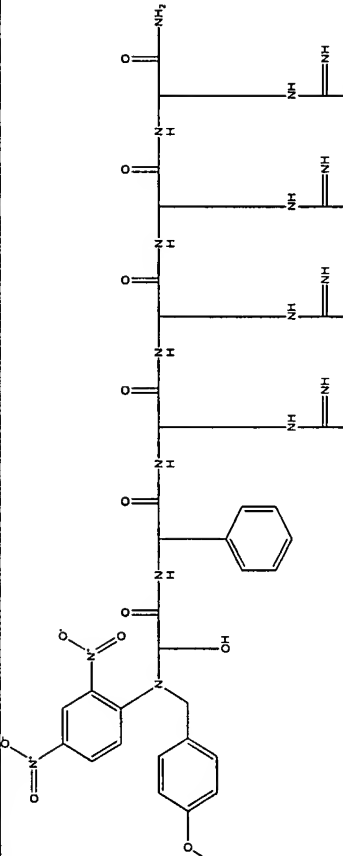
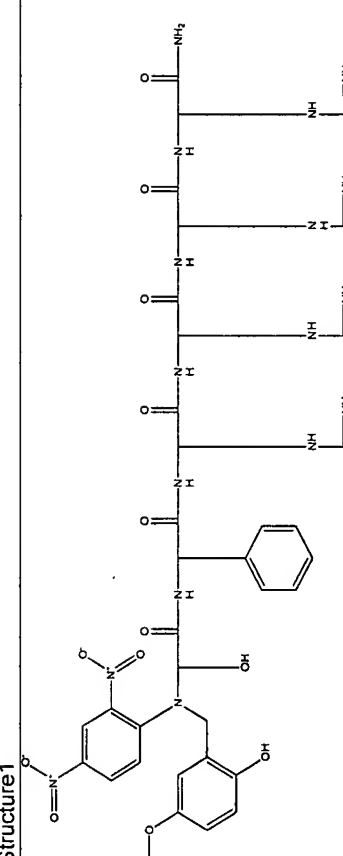
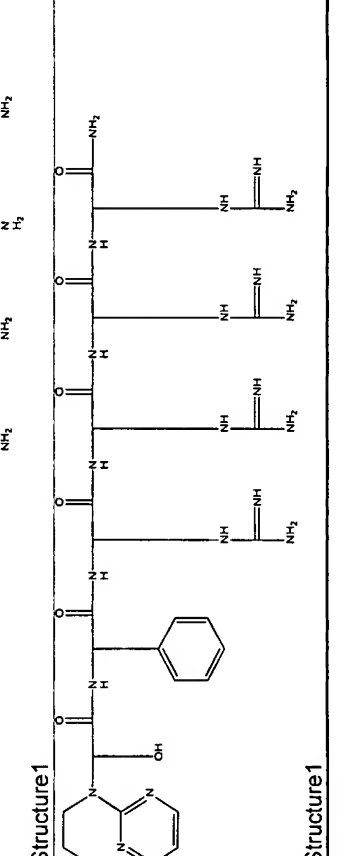
	C51H78N22O12	1191.3174 <10%	
	C51H78N22O11	1175.318 <10%	
	C49H74N22O13	1179.2632 <10%	

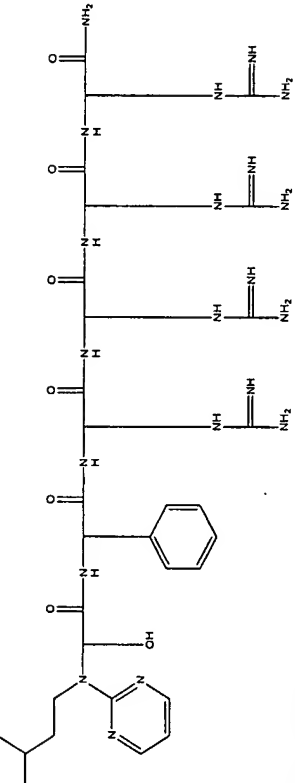
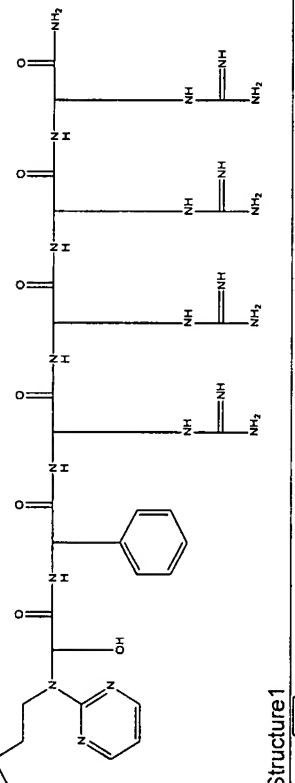
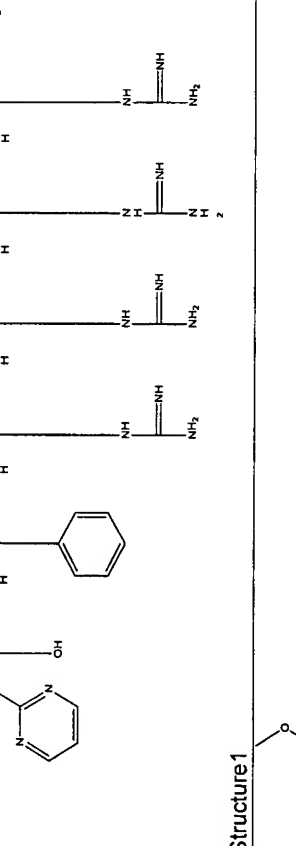
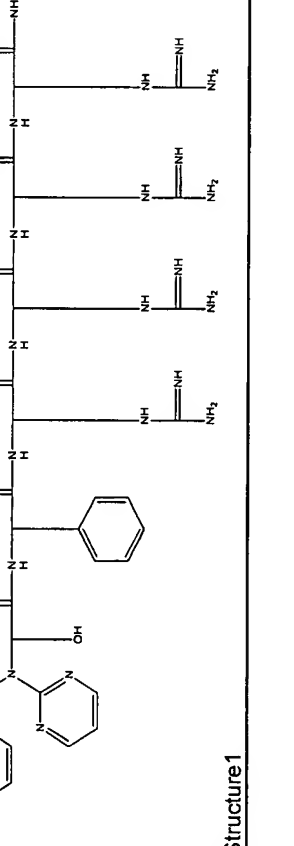
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 <p>Structure 1</p>	C49H71Cl2N21O11	1201.14 <10%	

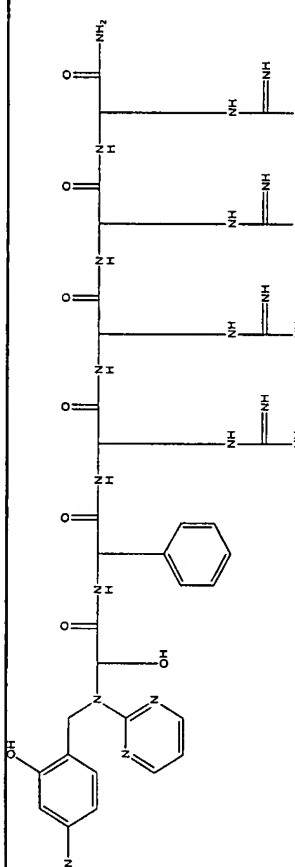
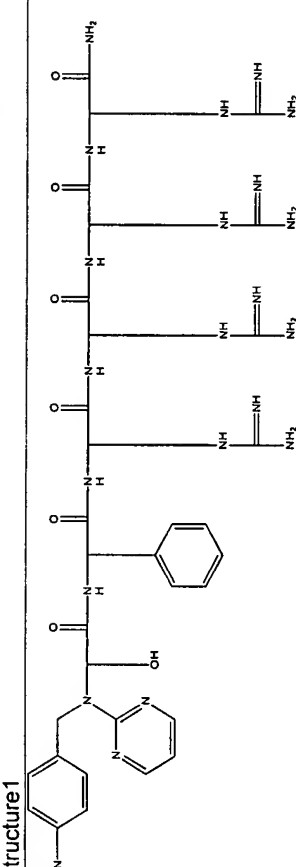
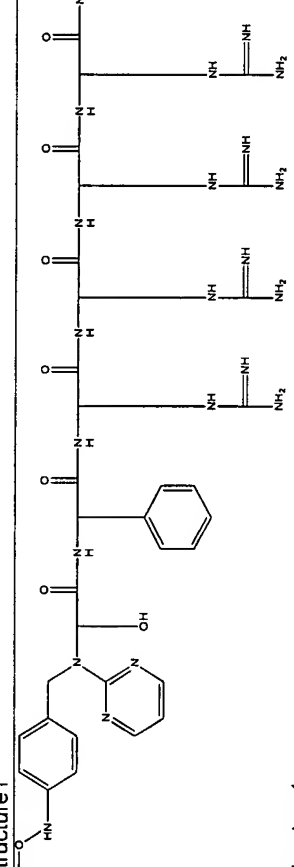
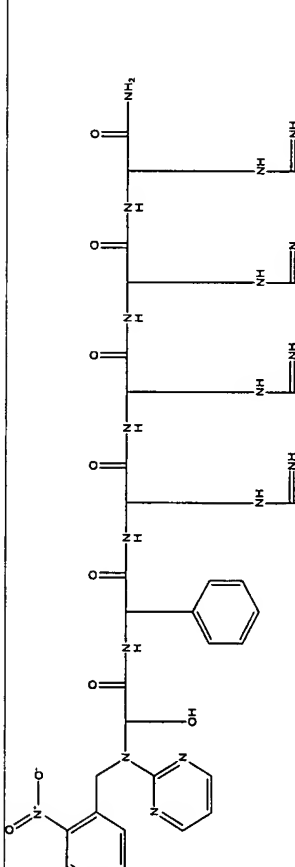
	C49H73N23O15	1224.2608	<10%
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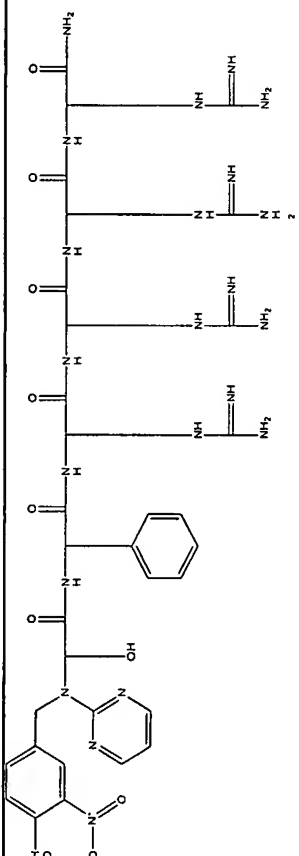
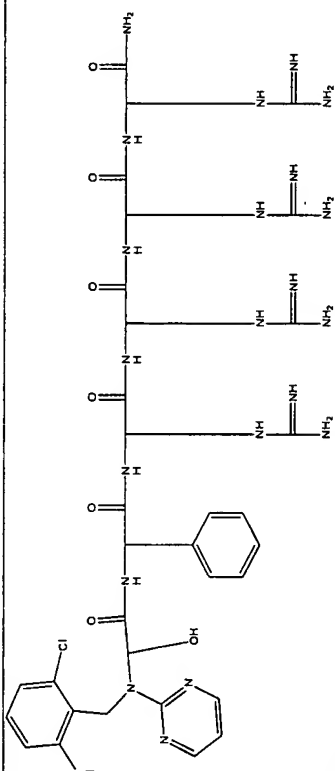
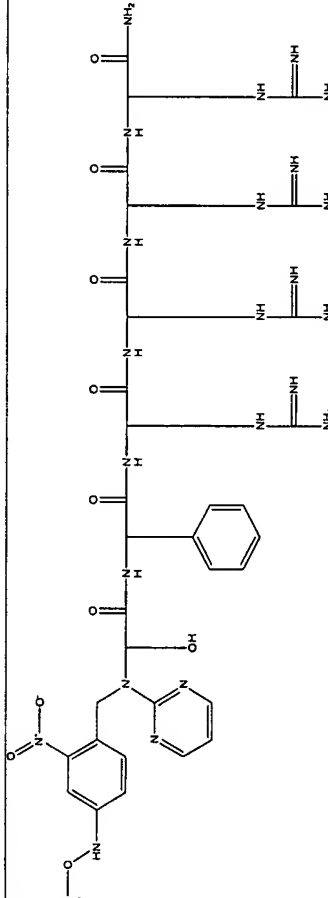
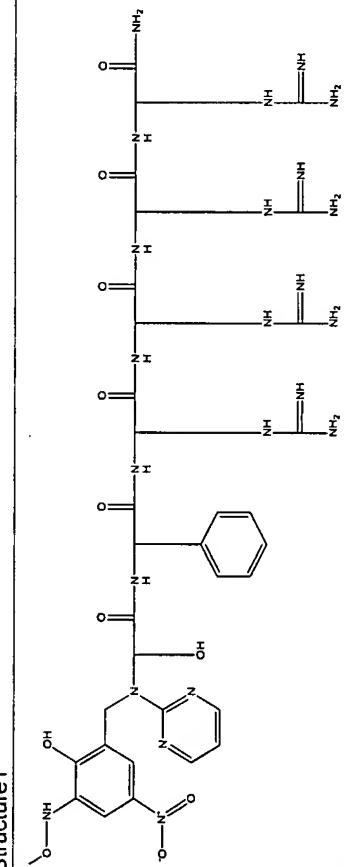
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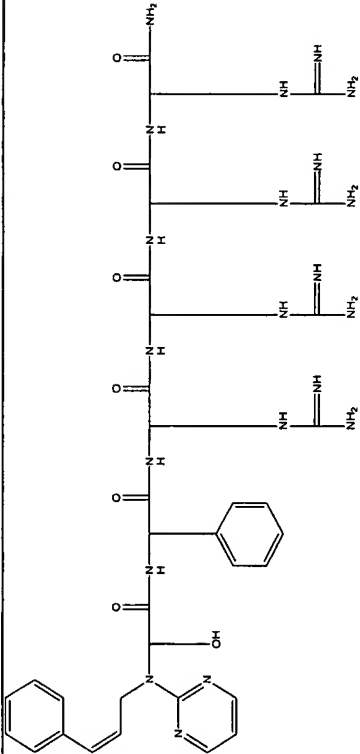
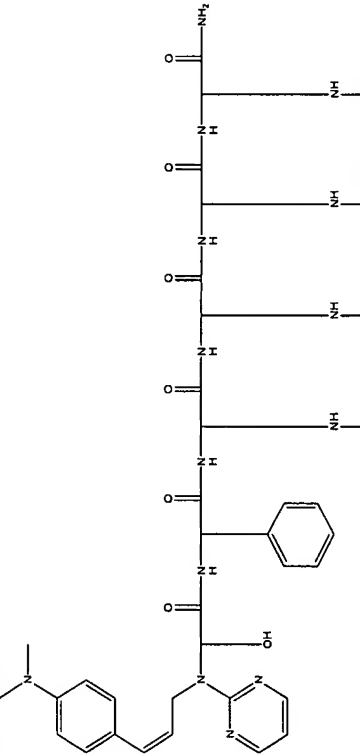
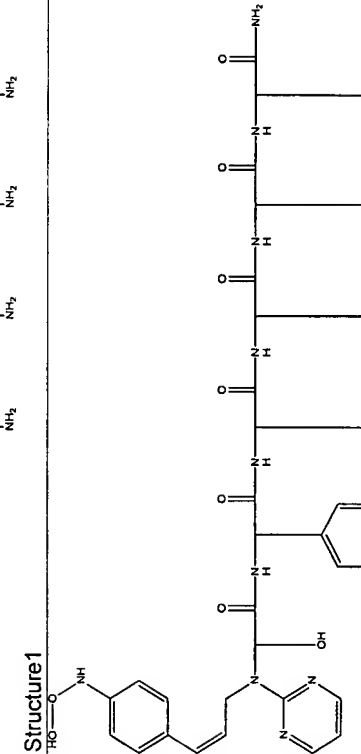
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 <p>Structure 1</p>	C57H77N21O11	1232.3694	<10%

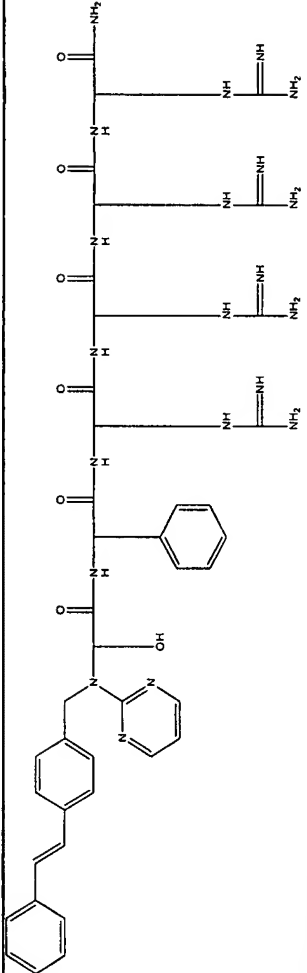
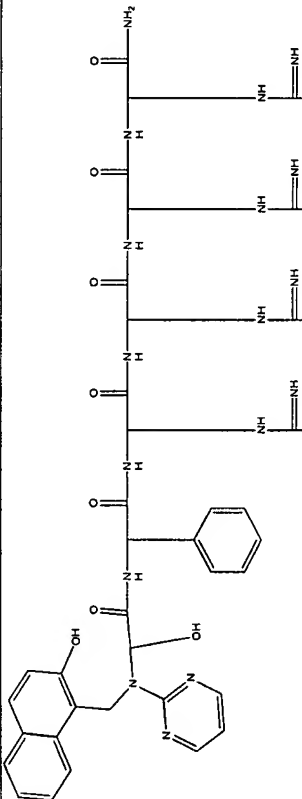
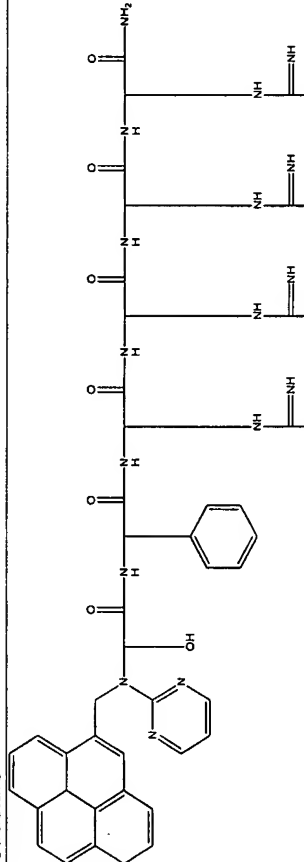
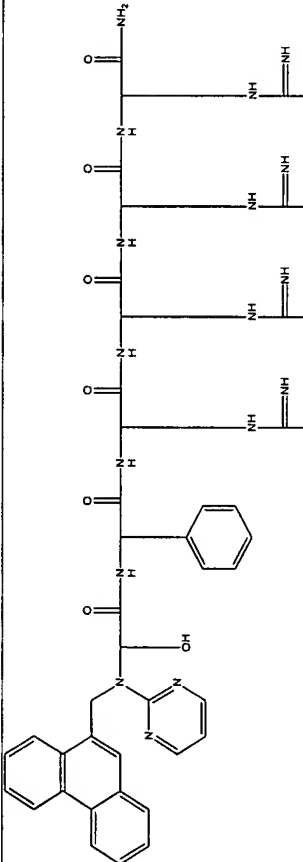
 <p>Structure 1</p>	C57H77N21O11	1232.3694	<10%
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 <p>Structure 1</p>	C50H75N21O13	1178.2754	<10%
 <p>Structure 1</p>	C43H73N21O7	996.1862	<10%

 Structure 1	C45H77N21O7	1024.2398 <10%	
 Structure 1	C46H79N21O7	1038.2666 <10%	
 Structure 1	C47H73N21O8	1060.2296 <10%	
 Structure 1	C49H77N21O9	1104.2826 <10%	

 <p>Chemical structure of a peptide derivative. The backbone consists of a 4-hydroxyphenyl group linked to a pyridine ring, which is further linked to a hydroxyl group. The side chain is a peptide chain with four residues, each containing an amide bond and a terminal amino group.</p>	C49H78N22O8	1103.2978 <10%
 <p>Chemical structure of a peptide derivative. The backbone consists of a 4-hydroxyphenyl group linked to a pyridine ring, which is further linked to a hydroxyl group. The side chain is a peptide chain with four residues, each containing an amide bond and a terminal amino group.</p>	C49H78N22O7	1087.2984 <10%
 <p>Chemical structure of a peptide derivative. The backbone consists of a 4-hydroxyphenyl group linked to a pyridine ring, which is further linked to a hydroxyl group. The side chain is a peptide chain with four residues, each containing an amide bond and a terminal amino group.</p>	C47H74N22O9	1091.2436 <10%
 <p>Chemical structure of a peptide derivative. The backbone consists of a 4-hydroxyphenyl group linked to a pyridine ring, which is further linked to a hydroxyl group. The side chain is a peptide chain with four residues, each containing an amide bond and a terminal amino group.</p>	C47H72N22O9	1089.2278 <10%

 <p>Structure 1</p>	C47H72N22O10	1105.2272	<10%
 <p>Structure 1</p>	C47H71Cl2N21O7	1113.1204	<10%
 <p>Structure 1</p>	C47H73N23O11	1136.2412	<10%
 <p>Structure 1</p>	C47H73N23O12	1152.2406	<10%

 <p>Structure 1</p>	C49H75N21O7	1070.268	<10%
 <p>Structure 1</p>	C51H80N22O7	1113.3362	<10%
 <p>Structure 1</p>	C49H76N22O9	1117.2814	<10%

 <p>Structure 1</p>	C55H79N21O7	1146.3656 <10%	
 <p>Structure 1</p>	C51H75N21O8	1110.2894 <10%	
 <p>Structure 1</p>	C57H79N21O7	1170.3876 <10%	
 <p>Structure 1</p>	C55H77N21O7	1144.3498 <10%	

	C55H77N21O7	1144.3498 <10%	
<p>Structure 1</p>	C48H75N21O8	1074.2564 <10%	
<p>Structure 1</p>	C48H75N21O9	1090.2558 <10%	

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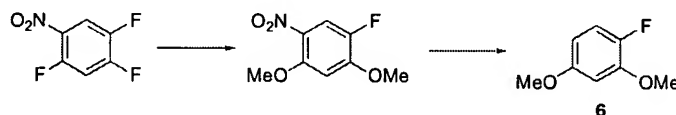
Supporting Information

Experimental

General Procedures. For all compounds, ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker AC-300 (300 MHz) NMR spectrometer. Proton and carbon chemical shifts are reported relative to TMS using either TMS or the residue solvent signal as internal standard. Carbon NMRs are proton-decoupled, and coupling constants to fluorine are not reported. Fluorine chemical shifts are reported relative to CF_3COOH (-78.5 ppm) as an external standard. Electrospray mass spectra (ESI) data were obtained from the Laboratory for Macromolecular Analysis and Proteomics of the Albert Einstein College of Medicine.

All moisture and air sensitive experiments were performed under a positive pressure of N_2 or Ar in oven dried glassware. Reagent and anhydrous solvents were bought from Aldrich Chemical Company and used without further purification.

1,3-Dimethoxy-4-fluorobenzene (6). See Wei-Chuan Sun, Kyle R. Gee, Dieter H. Klaubert and Richard P. Haugland; J. Org. Chem. 1997, 62, 6469-6475.



5-Fluoro-2,4-dimethoxy-benzonitrile. Sodium methoxide (25% wt in MeOH, 32 mL) was added dropwise to a solution of 2,4,5-trifluorobenzonitrile (10g, 63.7 mmol) in MeOH (160 mL) under nitrogen at 0 °C. The resulting reaction mixture was stirred at reflux for 48 h. The reaction was then quenched with 1 M citric acid and the MeOH was removed *in vacuo*. The residue was taken up in EtOAc, washed with brine, dried over Na_2SO_4 , concentrated *in vacuo* and recrystallized from EtOAc/hexane to furnish the desired product in 95% yield (11 g). ^1H NMR (300 MHz, CDCl_3) δ 7.25 (d, 1 H, $J = 10.2$ Hz), 6.52 (d, 1 H, $J = 6.8$ Hz), 3.97 (s, 3 H), 3.93 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.3, 159.2, 152.8, 152.6, 147.6, 144.4, 119.8, 119.5, 115.8, 115.7, 97.4, 97.3, 92.1, 92.0, 56.6, 56.5; ^{19}F NMR (282 MHz, CDCl_3) δ -143.4 (dd, 1 F); mass spectrum, calculated for $\text{C}_9\text{H}_8\text{FNO}_2$ (MH^+) 182.1, Found 182.1.

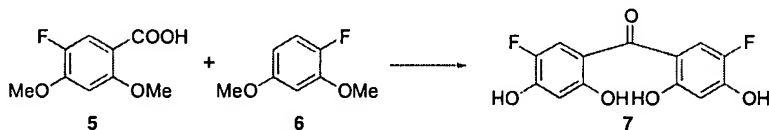


5-Fluoro-2,4-dimethoxy-benzoic acid (5). A solution of 3.1 g (17.2 mmol) of 2,4-dimethoxy-5-fluorobenzonitrile and 100 mL of 6N aqueous sodium hydroxide in 200 mL of methanol was stirred at reflux overnight, cooled to 0 °C, acidified to pH 1 - 2 with 6N aqueous hydrochloric acid, and partitioned between ethyl acetate and brine. The organic extract was dried over

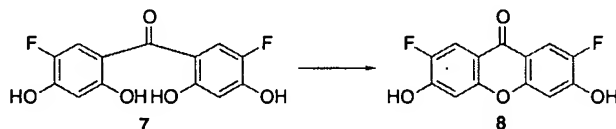
Na₂SO₄, and the solvents were removed *in vacuo* to give crude 2,4-dimethoxy-5-fluorobenzoic acid as a light-yellow solid. Recrystallization from ethyl acetate and hexane afforded 3.2 g (93%) of **5** as a white solid. ¹H NMR (300 MHz, DMSO-d₆) δ 12.4 (s, 1 H), 7.49 (d, 1 H, *J* = 12 Hz), 6.83 (d, 1 H, *J* = 7.2 Hz), 3.92 (s, 3 H), 3.84 (s, 3 H); ¹³C NMR (75 MHz, DMSO-d₆) δ 165.5, 165.5, 156.7, 151.1, 151.0, 146.3, 143.2, 117.9, 117.6, 111.2, 111.1, 99.3, 56.6, 56.4; ¹⁹F NMR (282 MHz, DMSO-d₆) δ -146.2 (dd, 1F); mass spectrum, calculated for C₉H₉FO₄ (MH⁺) 201.1, Found 200.9.



5,5'-difluoro-2,2',4,4'-tetrahydroxybenzophenone (7). 2,4-dimethoxy-5-fluorobenzoic acid **5** (5.4 g, 27 mmol) in dry CH₂Cl₂ (100 mL) was treated with 10.6 mL of oxalyl chloride under an Ar atmosphere and stirred at room temperature overnight. The excess reagent and solvent were removed under reduced pressure. The residue, 2,4-dimethoxy-5-fluorobenzoyl chloride, was redissolved in anhydrous CH₂Cl₂ (125 mL). 1,3-dimethoxy-4-fluorobenzene **6** (3.29 mL, 26 mmol) and AlCl₃ (10.8 g, 81 mmol) were added at 0 °C. After stirring at 0 °C for 1 h, the reaction mixture was allowed to warm to room temperature for 67 h, the mixture was then hydrolyzed with 1M HCl (300 mL) at 0 °C and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with 30% - 40% EtOAc in hexane to yield **7** (3.3 g, 44%) as a yellow solid. ¹H NMR (300 MHz, MeOH-d₄) 7.14 (d, 2 H, *J* = 11.5 Hz), 6.46 (d, 2 H, *J* = 7.4 Hz); ¹³C NMR (75 MHz, MeOH-d₄) δ 199.1, 159.0, 152.9, 152.7, 147.7, 144.5, 119.2, 118.9, 114.2, 114.1, 106.1, 106.0; ¹⁹F NMR (282 MHz, MeOH-d₄) δ -149.8 (dd, 2F).

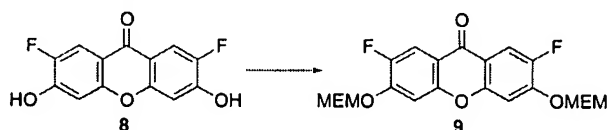


2,7-Difluoro-3,6-dihydroxy-xanthen-9-one (8). Compound **7** (0.75 g, 2.66 mmol) was heated in a sealed tube with H₂O (30 mL) at 200 - 220 °C for 2 - 3 h. On cooling, 2,7-difluoro-3,6-dihydroxyxanthone **8** precipitated out. The product was collected by filtration and washed with H₂O to give **8** (0.58 g, 83%) as a light yellow solid. ¹H NMR (300 MHz, DMSO-d₆) δ 11.4 (s, 2 H), 7.67 (d, 2 H, *J* = 10.9 Hz), 6.96 (d, 2 H, *J* = 7.1 Hz); ¹³C NMR (75 MHz, DMSO-d₆) δ 173.1, 153.1, 152.0, 151.8, 150.4, 147.2, 112.6, 112.5, 111.1, 110.8, 104.7, 104.6; ¹⁹F NMR (282 MHz, DMSO-d₆) δ -139.0 (dd, 2F); mass spectrum, calculated for C₁₃H₆F₂O₄ (MH⁺) 265.0, Found 264.9.

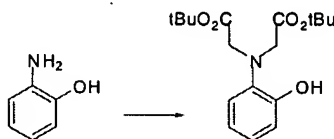


2,7-Difluoro-3,6-bis-(2-methoxyethoxymethoxy)-xanthen-9-one (9). A cloudy solution of **8** (2.4 g, 9.1 mmol) in dry THF (50 mL) was treated with sodium hydride (1.1 g, 45.8 mmol) at

0°C under an Ar atmosphere. The mixture was stirred at 0°C for 30 min and then 2-methoxyethoxymethyl chloride (5.2 mL, 45.8 mmol) was added. The mixture was stirred at 0°C for an additional 30 min and then warmed to room temperature overnight. The reaction mixture was cooled to 0°C, quenched with 1M citric acid (50mL), and then extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with CH₂Cl₂/hexane/EtOAc = 1:1:0.4 to yield 2.6 g (65%) of **9** as a white solid. *R_f* = 0.47 (in CH₂Cl₂/hexane/EtOAc = 1:1:0.4); ¹H NMR (300 MHz, CDCl₃) δ 7.91 (d, 2 H, *J* = 10.6 Hz), 7.28 (d, 2 H, *J* = 6.5 Hz), 5.46 (s, 4 H), 3.91 (m, 4 H), 3.60 (m, 4 H), 3.39 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 174.4, 153.3, 153.2, 151.4, 151.0, 150.9, 148.2, 115.2, 115.1, 111.8, 111.6, 104.8, 94.2, 71.3, 68.6, 59.0; ¹⁹F NMR (282 MHz, CDCl₃) δ -137.0 (dd, 2 F); mass spectrum, calculated for C₂₁H₂₂F₂O₈ (MH⁺) 441.1, Found 441.0.

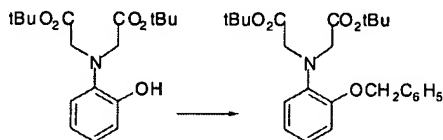


[*tert*-Butoxycarbonylmethyl-(2-hydroxy-phenyl)-amino]-acetic acid *tert*-butyl ester. A solution of 2-aminophenol (5.0 g, 45.8 mmol) and NaI (3.44 g, 23 mmol) in dry CH₃CN (150 mL) was treated with 1,8-bis(dimethylamino) naphthalene (21.6 g, 100.8 mmol) followed by *t*-butyl bromoacetate (14.2 mL, 96.2 mmol) under an Ar atmosphere and stirred at reflux overnight. After the mixture was cooled to room temperature, the precipitated salts were filtered off and washed with additional EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with CH₂Cl₂/hexane/EtOAc = 1:4:0.2 to yield 12.3 g (80%) of the desired product as a light yellow oil. *R_f* = 0.3 (in CH₂Cl₂/hexane/EtOAc = 1:4:0.2); ¹H NMR (300 MHz, CDCl₃) δ 7.29 (dd, 7.9 and 1.5 Hz, 1 H), 7.07 (m, 1 H), 6.94 (dd, 8.1 and 1.5 Hz, 1 H), 6.79 (m, 1 H), 5.30 (s, 1 H), 3.74 (s, 4 H), 1.46 (s, 18 H); ¹³C NMR (75 MHz, CDCl₃) δ 171.2, 153.6, 137.4, 127.3, 126.0, 119.9, 115.6, 81.9, 57.0, 28.0; mass spectrum, calculated for C₁₈H₂₇NO₅ (MH⁺) 338.2, Found 337.9.

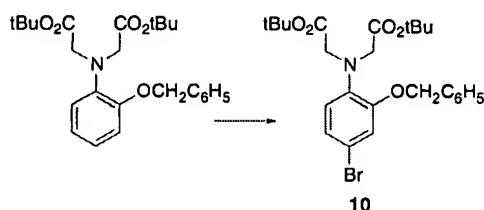


[(2-Benzyloxy-phenyl)-*tert*-butoxycarbonylmethyl-amino]-acetic acid *tert*-butyl ester. A solution of [*tert*-Butoxycarbonylmethyl-(2-hydroxy-phenyl)-amino]-acetic acid *tert*-butyl ester (7.4 g, 21.9 mmol) in dry THF (50 mL) was treated with sodium hydride (0.81 g, 33.8 mmol) at 0°C under an Ar atmosphere. After stirring at 0°C for 30 min, benzyl bromide (3.9 mL, 32.7 mmol) was added. The mixture was stirred at 0°C for another 30 min and then warmed to room temperature overnight. The reaction mixture was quenched with H₂O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with CH₂Cl₂/hexane/EtOAc = 1:4:0.2 to yield 6.3 g (67%) of the desired product as a colorless oil. *R_f* = 0.33 (in CH₂Cl₂/hexane/EtOAc = 1:4:0.2); ¹H NMR (300 MHz, CDCl₃) δ 7.45 - 7.28 (m, 5 H),

6.84 (m, 4 H), 5.12 (s, 2 H), 4.08 (s, 4 H), 1.40 (s, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.5, 150.5, 139.6, 137.5, 128.4, 127.6, 127.2, 121.9, 121.4, 119.4, 114.7, 81.0, 70.9, 54.6, 28.0; mass spectrum, calculated for $\text{C}_{25}\text{H}_{33}\text{NO}_5$ (MH^+) 428.2, Found 427.9.

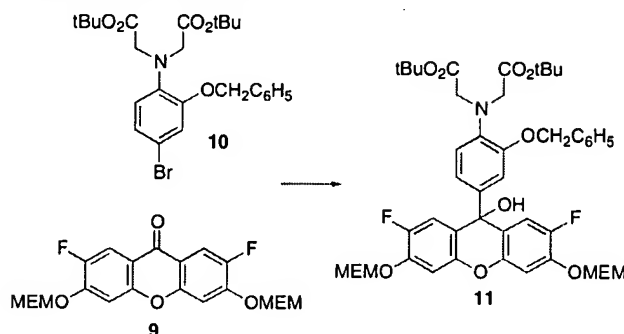


[(2-Benzoyloxy-4-bromo-phenyl)-tert-butoxycarbonylmethyl-amino]-acetic acid tert-butyl ester (10). To a -78°C solution of [(2-Benzoyloxy-phenyl)-tert-butoxycarbonylmethyl-amino]-acetic acid tert-butyl ester (6.3 g, 14.7 mmol) in CH_2Cl_2 (100 mL) was added pyridine (1.8 mL, 22.1 mmol) followed by bromine (0.91 mL, 17.6 mmol) under an Ar atmosphere. After 30 min, the mixture was allowed to warm to room temperature and then washed with water, 5% sodium bicarbonate, and brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with $\text{CH}_2\text{Cl}_2/\text{hexane}/\text{EtOAc} = 1:4:0.2$ to yield 5.9 g (79 %) of **10** as a white solid. $R_f = 0.43$ (in $\text{CH}_2\text{Cl}_2/\text{hexane}/\text{EtOAc} = 1:4:0.2$); ^1H NMR (300 MHz, CDCl_3) δ 7.45 - 7.26 (m, 5 H), 6.99 (m, 2 H), 6.73 (m, 1 H), 5.09 (s, 2 H), 4.04 (s, 4 H), 1.41 (s, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.1, 151.1, 138.7, 136.6, 128.6, 127.9, 127.4, 124.1, 120.5, 117.6, 113.7, 81.2, 71.2, 54.5, 28.0; mass spectrum, calculated for $\text{C}_{25}\text{H}_{32}\text{BrNO}_5$ (MH^+) 506.2, Found 505.8.

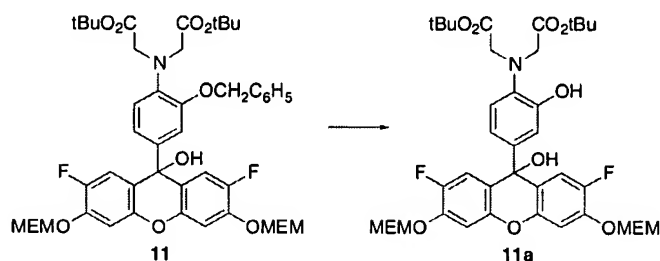


[(2-Benzoyloxy-4-[2,7-difluoro-9-hydroxy-3,6-bis-(2-methoxyethoxymethoxy)-9H xanthen-9-yl]-phenyl)-tert-butoxycarbonylmethyl-amino]-acetic acid tert-butyl ester (11). The bromide **10** (807 mg, 1.59 mmol) was dissolved in 20 mL THF/2-methyltetrahydrofuran (1:1) and cooled to -105°C in a liquid N_2 /diethyl ether bath. After stirring at -105°C for 10 min, 4.5 mL of tert-butyllithium (1.1 M in pentanes) was added dropwise. Stirring was continued for another 15 min. 2,7-difluoro-3,6-bis-(2-methoxy-ethoxymethoxy)-xanthen-9-one **9** (912 mg, 2.07 mmol) dissolved in THF (10 mL) was added dropwise to the reaction mixture. The mixture was stirred at -105°C for 30 min, the cooling bath removed, and the reaction solution was then stirred for an additional 15 min. The resulting mixture was added to 150 mL $\text{NH}_4\text{Cl}(\text{sat})$ and extracted twice with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with 50% EtOAc in hexane (with 0.1% Et_3N) to yield 956 mg (69%) of **11** as a orange-red oil. $R_f = 0.33$ (in 50% EtOAc/hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.32 - 7.27 (m, 5 H), 6.97 (d, 2 H, $J = 6.98$ Hz), 6.86 (m, 3 H), 6.72 (m, 2 H), 5.30 (s, 4 H), 5.05 (s, 2 H), 4.02 (s, 4 H), 3.85 (m, 4 H), 3.56 (m, 4 H), 3.36 (s, 6 H), 1.38 (s, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.5, 150.8, 149.3, 147.6, 145.6, 145.5, 145.4, 145.2, 140.5, 138.4, 136.9, 128.3, 127.7, 127.5, 119.9, 119.8, 119.3, 118.4, 115.2, 114.9, 113.0, 104.9, 94.5, 81.0, 71.4, 70.6, 69.7,

68.1, 58.9, 54.6, 28.0; ^{19}F NMR (282 MHz, CDCl_3) δ -139.0 (dd, 2 F); mass spectrum, calculated for $\text{C}_{46}\text{H}_{55}\text{F}_2\text{NO}_{13}$ (MH^+) 868.4, Found 867.8.

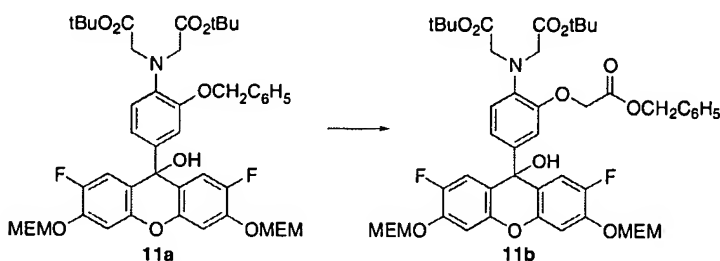


(*tert*-Butoxycarbonylmethyl- $\{4-[2,7$ -difluoro-9-hydroxy-3,6-bis-(2-methoxyethoxymethoxy)-9H-xanthen-9-yl]-2-hydroxy-phenyl}-amino)-acetic acid *tert*-butyl ester (**11a**). To a solution of **11** (956 mg, 1.1 mmol) in 95% ethanol (25 mL) and EtOAc (25 mL) was added 10% Pd/C (130 mg). The resulting mixture was stirred at room temperature overnight under H_2 (1 atm). The catalyst was then removed by filtration and, after evaporation to dryness, the crude product was purified by flash column chromatography, eluting with 40% EtOAc in hexane (with 0.1% Et_3N) to yield 671 mg (78%) of **11a** as a light yellow oil. R_f = 0.3 (in 40% EtOAc/hexane); ^1H NMR (300 MHz, CDCl_3) δ 8.1 (s, 1 H), 7.18 (d, 1 H, J = 8.0 Hz), 6.95 (d, 2 H, J = 7.2 Hz), 6.69 (m, 3 H), 6.57 (m, 1 H), 5.28 (s, 4 H), 4.94 (s, 1 H), 3.85 (m, 4 H), 3.69 (s, 4 H), 3.57 (m, 4 H), 3.38 (s, 6 H), 1.41 (s, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.2, 153.8, 150.6, 147.4, 146.5, 144.8, 144.4, 144.2, 136.3, 126.3, 119.6, 116.7, 116.6, 116.1, 115.8, 115.5, 105.9, 94.6, 81.9, 71.4, 68.0, 59.0, 56.9, 43.1, 27.9; ^{19}F NMR (282 MHz, CDCl_3) δ -140.4 (dd, 2 F); mass spectrum, calculated for $\text{C}_{46}\text{H}_{55}\text{F}_2\text{NO}_{13}$ (M-17) 761.3, Found 761.7.

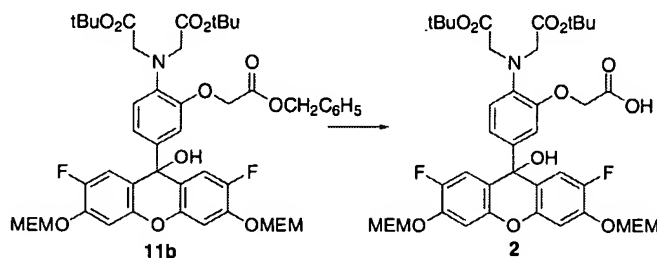


($\{2$ -Benzyloxycarbonylmethoxy-4-[2,7-difluoro-9-hydroxy-3,6-bis-(2-methoxyethoxymethoxy)-9H-xanthen-9-yl]-phenyl}-*tert*-butoxycarbonylmethyl-amino)-acetic acid *tert*-butyl ester (**11b**). A solution of **11a** (497 mg, 0.64 mmol) in DMF (10 mL) was treated with sodium hydride (18.5 mg, 0.77 mmol) at 0°C under an Ar atmosphere. After stirring at 0°C for 30 min, benzyl 2-bromoacetate (0.15 mL, 0.96 mmol) was added. The mixture was stirred at 0°C for another 30 min and then warmed to room temperature overnight. The solvent was evaporated to dryness and extracted with EtOAc/ H_2O . The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography, eluting with 40% EtOAc in Hexane (with 0.1% Et_3N) to yield 453 mg (76%) of **11b** as a light yellow oil. R_f = 0.28 (in 40% EtOAc/hexane); ^1H NMR

(300 MHz, CDCl₃) δ 7.32 (m, 5 H), 6.96 (d, 2 H, J = 7.2 Hz), 6.86 (d, 1 H, J = 8.4 Hz), 6.72 (dd, 1 H, J = 7.8 and 1.5 Hz), 6.59 (m, 3 H), 5.28 (s, 4 H), 5.15 (s, 2 H), 4.89 (s, 1 H), 4.64 (s, 2 H), 4.01 (s, 4 H), 3.86 (m, 4 H), 3.58 (m, 4 H), 3.39 (s, 6 H), 1.39 (s, 18 H); ¹³C NMR (75 MHz, CDCl₃) δ 170.3, 168.8, 150.7, 149.9, 147.5, 146.6, 146.5, 144.4, 144.3, 139.1, 138.9, 135.3, 128.6, 128.4, 128.3, 122.9, 120.0, 117.0, 116.9, 116.2, 116.1, 115.8, 105.9, 94.7, 81.2, 71.5, 68.1, 66.7, 66.6, 59.0, 54.5, 42.6, 28.0; ¹⁹F NMR (282 MHz, CDCl₃) δ -140.2 (dd, 2 F); mass spectrum, calculated for C₄₆H₅₅F₂NO₁₃ (M-17) 909.4, Found 910.1.



{2-(Bis-tert-butoxycarbonylmethyl-amino)-5-[2,7-difluoro-9-hydroxy 3,6-bis-(2-methoxyethoxymethoxy)-9H-xanthen-9-yl]-phenoxy}-acetic acid (2). To a solution of 11b (743 mg, 0.80 mmol) in 95% ethanol (25 mL) and EtOAc (25 mL) was added 10% Pd/C (135 mg). The resulting mixture was stirred at room temperature overnight under H₂ (1 atm). The catalyst was then removed by filtration and, after evaporation to dryness, the crude product was purified by flash column chromatography, eluting with 10% MeOH in CH₂Cl₂ to yield 595 mg (89%) of **2** as a red foaming solid. R_f = 0.43 (in 10% MeOH/CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 10.0 (br, 1 H), 6.93 (d, 2 H, J = 7.2 Hz), 6.86 (d, 1 H, J = 8.2 Hz), 6.71 (dd, 1 H, J = 8.2 and 1.3 Hz), 6.62 (m, 3 H), 5.24 (s, 4 H), 4.93 (s, 1 H), 4.53 (s, 2 H), 3.91 (s, 4 H), 3.83 (m, 4 H), 3.56 (m, 4 H), 3.35 (s, 6 H), 1.34 (s, 18 H); ¹³C NMR (75 MHz, CDCl₃) δ 171.0, 170.5, 150.6, 150.5, 147.4, 146.4, 146.3, 144.4, 144.2, 140.8, 138.7, 122.3, 120.7, 116.6, 116.5, 115.9, 115.6, 115.4, 105.9, 94.6, 81.7, 71.3, 67.9, 67.3, 58.8, 55.0, 42.7, 27.8; ¹⁹F NMR (282 MHz, CDCl₃) δ -140.0 (dd, 2 F); mass spectrum, calculated for C₄₆H₅₅F₂NO₁₃ (M-17) 819.3, Found 819.8.



H₂N-Ser(tBu)-Phe-[Arg(Mtr)]₄-cystamine-TentaGel Resin (12). Cystamine dihydrochloride (10 eq, 2.25 g) was added to a mixture of TentaGel S COOH resin (90 μ m, 5 g, 0.2 mmol/g), BOP (1.2 eq, 0.53 g), HOBT (1.2 eq, 0.184 g), N-methylmorpholine (NMM) (30 eq, 3.3 mL) in 20 mL DMF and subsequently shaken overnight at ambient temperature. The free amine substitution level was determined as 0.01 mmol/g. This low substitution level is ideal for our purposes since this not only ensures a higher coupling yield but, in addition, larger quantities of resin (with greater weight accuracy) can be subsequently introduced into the 96-well plates. The

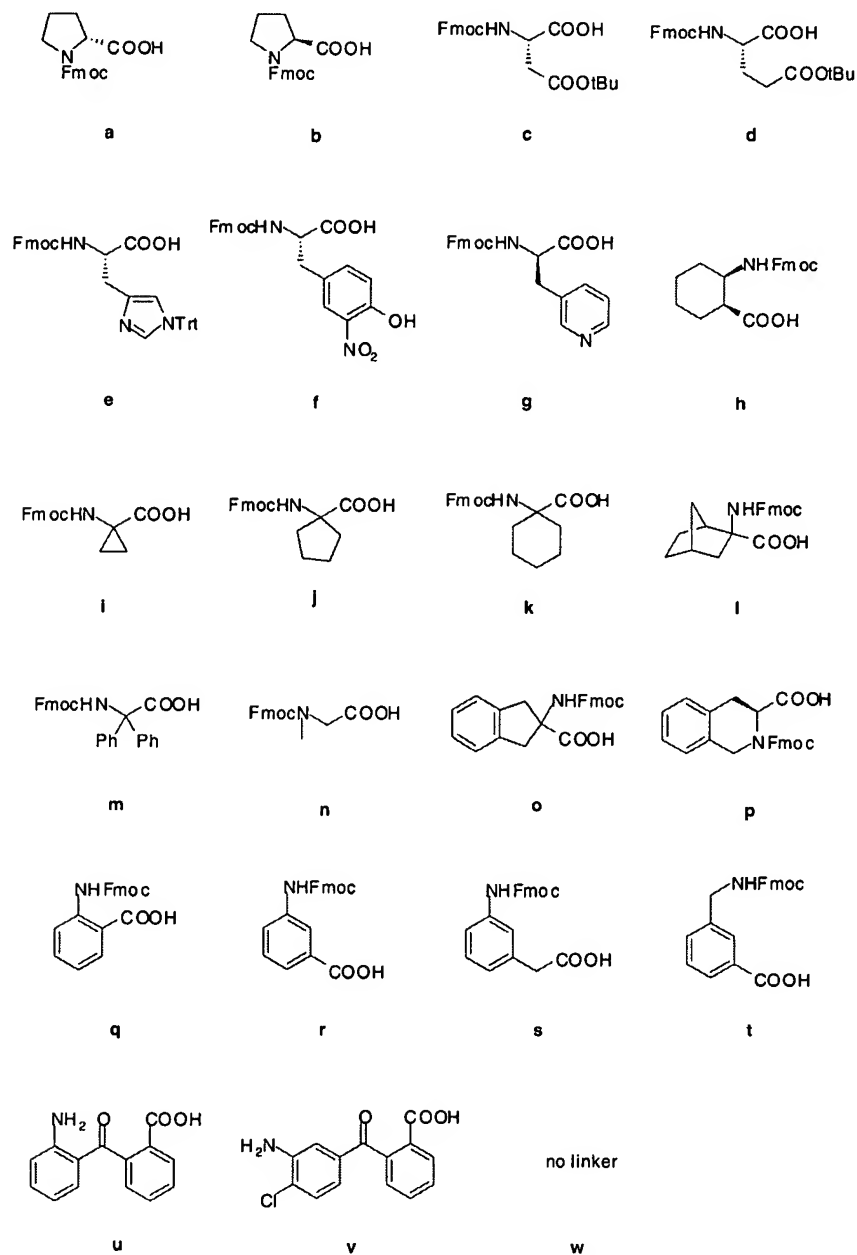
peptide NH₂-Ser(tBu)-Phe-[Arg(Mtr)]₄ was synthesized on the cystamine-substituted TentaGel resin using an Fmoc solid phase peptide synthesis protocol.

General protocol for the preparation of the fluorophore-peptide conjugates (3 and 14). Both compound **3** and the corresponding linker-based library **14** (23 compounds) were prepared using the same protocol, with the exception that the library members were synthesized in a solvent resistant 96-well filter plate. 10 mg of the peptide-TentaGel resin **12** was introduced into 23 individual wells of a 96-well filter plate. In addition, each well contained a Fmoc-linker-COOH (10 eq), *O*-benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (10 eq), 1-hydroxybenztriazole (10 eq), and *N*-methylmorpholine (20 eq) in 100 μ L DMF. A total of 22 different Fmoc-linker-COOH linkers were employed. One additional well was reserved for the species that does not contain a linker. The plate was shaken overnight and then each well was subjected to a series of wash steps (3 \times 200 μ L DMF, 3 \times 200 μ L water, 3 \times 200 μ L DMF, 3 \times 200 μ L CH₂Cl₂, 2 \times 200 μ L MeOH, 2 \times 200 μ L 50 mM Tris pH 7.5). The *N*-terminal Fmoc protecting group was removed via double exposure to 30% piperidine in DMF for 30 min and then each well was subjected to a series of wash steps (3 \times 200 μ L DMF, 3 \times 200 μ L water, 3 \times 200 μ L DMF, 3 \times 200 μ L CH₂Cl₂, 2 \times 200 μ L MeOH, 2 \times 200 μ L 50 mM Tris pH 7.5). The side chain protecting groups on the peptide were removed via treatment with 95% trifluoroacetic acid/2.5% thioanisole/2.5% H₂O at room temperature overnight to furnish **13**. Each well was subsequently subjected to a series of wash steps (3 \times 200 μ L DMF, 3 \times 200 μ L water, 3 \times 200 μ L DMF, 3 \times 200 μ L CH₂Cl₂, 2 \times 200 μ L MeOH, 2 \times 200 μ L 50 mM Tris pH 7.5). {2-(Bis-tert-butoxycarbonylmethyl-amino)-5-[2,7-difluoro-9-hydroxy 3,6-bis-(2-methoxy-ethoxymethoxy)-9H-xanthen-9-yl]-phenoxy}-acetic acid (**4**) (5 eq) was coupled to the peptide-TentaGel resin **13** under standard conditions [*O*-benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (5 eq), 1-hydroxybenztriazole (5 eq), and *N*-methylmorpholine (10 eq) in 100 μ L DMF]. The attached xanthene was then deprotected and fully aromatized via exposure to 95% trifluoroacetic acid/5% H₂O. The fluorophore-peptide conjugates were cleaved from the disulfide-containing resin with 10 mM dithiothreitol (DTT) in Tris buffer (1 \times 200 μ L for 1 Hr; 2 \times 150 μ L for 1 hr each) and filtered into a receiving set of 96-well plates using a vacuum manifold to furnish the library **14**.

Mass spectrum, calculated for **14a** 1544.7, Found 1624.0 (M + 79.9); calculated for **14b** 1544.7, Found 1544.0; calculated for **14c** 1562.6, Found 1562.0; calculated for **14d** 1576.7, Found 1576.0; calculated for **14e** 1584.7, Found 1584.0; calculated for **14f** 1655.7, Found 1657.0 (M + 2); calculated for **14g** 1595.7, Found 1596.0; calculated for **14h** 1572.7, Found 1572.0; calculated for **14i** 1530.6, Found 1530.0; calculated for **14j** 1558.7, Found 1558.0; calculated for **14k** 1572.7, Found 1574.0; calculated for **14l** 1584.0, Found 1584.0 (M + 2); calculated for **14m** 1518.0, Found 1518.0; calculated for **14n** 1517.7, Found 1518.0; calculated for **14o** 1606.7, Found 1607.0; calculated for **14p** 1606.7, Found 1607.0 (M + 2); calculated for **14q** 1566.7, Found no identifiable mass ion; calculated for **14r** 1566.7, Found 1566.0; calculated for **14s** 1580.7, Found 1581.0; calculated for **14t** 1580.7, Found 1581.0; calculated for **14u** 1670.7, Found no identifiable mass ion; calculated for **14v** 1796.2, Found no identifiable mass ion; calculated for **14w** 1447.5, Found 1447.0;



The 22 linker monomers (plus compound w) employed in the preparation of library 14:



Protein kinase C assay. The kinase-catalyzed reaction was performed in triplicate at 30 °C and initiated by addition of ATP to a solution of PKC α and fluorophore-appended peptide substrate 3 (except in the case of the library, where the assays were performed in a 96 well plate using a fluorescence plate reader). Final conditions: 62.5 mM HEPES, 3 mM MgCl₂, 0.3 mM CaCl₂, 0.1 mM EGTA, 1 mM DTT, 0.5 μ g/mL phosphatidylserine, 0.1 μ g/mL diacylglycerol, 1 mM ATP, and 13 nM PKC α (pH 7.4). After the addition of ATP, the solution was gently mixed and the time-dependent change in fluorescent intensity ($\lambda_{\text{excitation}} = 494$ nm; $\lambda_{\text{emission}} = 521$ nm) continuously monitored with a Photon Technology QM-1 spectrofluorimeter.

Ca²⁺ titration assay. The Ca²⁺ Calibration Kit #2 (purchased from Molecular Probes) was employed for these studies. The fluorescent peptide was dissolved in two buffers, one without (SOLUTION A: 10 mM MOPs, 100 mM KCl, 10 mM EGTA, pH 7.2) and one with (SOLUTION B: 10 mM MOPs, 100 mM KCl, 10 mM CaEGTA, pH 7.2) Ca²⁺. The final concentration of the peptide in both buffers was 1 μ M. Solution A was (200 μ L) added to the microcuvette and the fluorescence was recorded ($\lambda_{\text{excitation}} = 494$ nm; $\lambda_{\text{emission}} = 521$ nm). This was the fluorescence intensity with 0 Ca²⁺. A series of solutions containing the following free Ca²⁺ concentrations (based on the K_d of CaEGTA at pH 7.2 = 150.3 nM) was prepared: 0.038 μ M, 0.065 μ M, 0.1 μ M, 0.15 μ M, 0.225 μ M, 0.351 μ M, 0.602 μ M, 1.35 μ M, and 39.8 μ M.

